EAST Search History

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S2	112	"5512549"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	AND	ON	2007/01/26 19:06
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LI
          24309 S "FREE RADICAL SCAVENGER"
44707 S ISCHEM###### AND EVENT
L4 158841 S REPERFUSION
L5 183126 S CARDIAC INTERVENTION OR (ANGIOPLASTY OR
"CORONARY BY PASS" OR
L6 110219 S CARDIAC AND (ISCHEMIA OR REPERFUSION OR
"CONGESTIVE HEART FAI
           355 S METABOLIC INTERVENTION
74695 S ARRHYTHMIA AND (TREAT##### OR PREVENT########)
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              4695 $ ARRHYTHMIA AND (TREAT##
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1 $ L1 AND L2 AND PD<=20031219
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=> S Nephropathy OR ("END Stage renal disease") OR ESRD
L22 139696 NEPHROPATHY OR ("END STAGE RENAL DISEASE") OR ESRD
=> S Endothelial Function
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22772 ENDOTHELIAL FUNCTION

=> S ProteinUria L24 82699 PROTEINURIA

L18

L19 L20

S Glomerulosclerosis L25 21397 GLOMERULOSCLEROSIS

=> s Diabetes OR "Insulin resistance" OR hypertension L26 1521989 DIABETES OR "INSULIN RESISTANCE" OR HYPERTENSION

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139696 S NEPHROPATHY OR ("END STAGE RENAL DISEASE") OR ESRD
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                                   1 S L1 AND L23 AND PD<=20031219
1 S L1 AND L24 AND PD<=20031219
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1792 S L1 AND L26 AND PD<=20031219
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  L31
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  in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
 or the STAGUIDE HIE FOR HINDHAMAN OF COMMENTAL STATEMENTS OF THE HIERONG HIERO
  In a multifile environment, a format can only be used if it is valid
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1 9302 S EXEMBIN OR GLF-1 OK ("GLUCAGON-LIKE AGONS
L2 24309 S "FREE RADICAL SCAVENGER"
L3 44707 S ISCHEM##### AND EVENT
L4 158841 S REPERFUSION
L5 183126 S CARDIAC INTERVENTION OR (ANGIOPLASTY OR
"CORONARY BY PASS" OR
L6 110219 S CARDIAC AND (ISCHEMIA OR REPERFUSION OR "CONGESTIVE HEART FAI
         355 S METABOLIC INTERVENTION
74695 S ARRHYTHMIA AND (TREAT##### OR PREVENT########
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L27 ANSWER I OF 14 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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  ACCESSION NUMBER: 2003:390202 BIOSIS <<LOGINID::20070124>> DOCUMENT NUMBER: PREV200300390202
                            The glucagon-like peptides: A double-edged therapeutic
                       sword?.
 AUTHOR(S): Perry, TracyAnn [Reprint Author]; Greig, Nigel H.
CORPORATE SOURCE: Section of Drug Design and Development, Laboratory of
Neurosciences, Gerontology Research Center, National
Institute on Aging, National Institutes of Health, 5600
Nathan Shock Drive, Baltimore, MD, 21224, USA
perryt@grc.nia.nih.gov

SOURCE: Trends in Pharmacological Sciences, (July 2003)

Vol. 24, No. 7, pp. 377-383. print.

ISSN: 0165-6147 (ISSN print).

DOCUMENT TYPE: Article

General Review; (Literature Review)

LANGUAGE: English

ENTRY DATE:
                                English
Entered STN: 27 Aug 2003
  ENTRY DATE:
                      Last Updated on STN: 27 Aug 2003
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L33 9 DUP REM L27 (5 DUPLICATES REMOVED)
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=> Dup Rem 132 PROCESSING COMPLETED FOR L32 L34 9 DUP REM L32 (4 DUPLICATES REMOVED) => D Ibib All L28 L28 ANSWER I OF I CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:447519 CAPLUS <<LOGINID::20070124>>
DOCUMENT NUMBER: 139:255595 Antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive rats Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly, Annette; Ditter, Katie; Mistry, Mahesh; Roman, Richard AUTHOR(S): SOURCE: Department of Physiology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA CORPORATE SOURCE: Journal of Hypertension (2003), 21(6), 1125-1135 SOURCE: CODEN: JOHYD3; ISSN: 0263-6352 PUBLISHER: Lippincott Williams & Wilkins

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DOCUMENT TYPE:
                                                                                                        Journal
 LANGUAGE: English
AN 2003:447519 CAPLUS << LOGINID::20070124>>
 DN 139:255595
ED Entered STN: 11 Jun 2003
  TI Antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive
 AU Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly, Annette; Ditter,
Katie; Mistry, Mahesh; Roman, Richard J.
  CS Department of Physiology, Medical College of Wisconsin, Milwaukee, W1,
 SO Journal of Hypertension (2003), 21(6), 1125-1135
CODEN: JOHYD3; ISSN: 0263-6352
PB Lippincott Williams & Wilkins
DT Journal
 LA English
LA Engiss

CE 2-6 (Mammalian Hormones)

AB Dahl salt-sensitive (Dahl S) rats exhibit many phenotypic traits associated with salt-sensitive hypertension in man. Specifically, they are salt-sensitive, insulin-resistant and hyperlipidemic. They also develop endothelial dysfunction, cardiac injury and glomerulosclerosis. Insulin resistance is linked to hypertension, renal and cardiac damage and exhibited designation. Thus, an agent that had direction to and can
        resistance is linked to hypertension, renal and cardiac damage and endothelial dysfunction. Thus, an agent that has diuretic action and can improve insulin resistance, like recombinant glucagon-like peptide-1(7-36)amide (rGLP-1), may have an antihypertensive effect. To determine whether chronic administration of rGLP-1 attenuates the development of hypertension, endothelial dysfunction and/or hypertension-induced renal and cardiac end organ damage in Dahl S rats. Mean arterial pressure (MAP) and urinary excretion of protein and albumin were measured in Dahl S rats before and after they were fed a 8% NaCl diet and infused with rGLP-1 (1 mg/kg per min, i.v.) or vehicle for 14 days. At the end of the study, the degree of renal and cardiac injury was histoil, assessed and endothelium-dependent relaxing function was studied using aortic rings. In other rats, the effects of rGLP-1 on sodium and water balance and plasma glucose and insulin levels for the first 3 days following a step change in sodium intake from a 0.1% NaCl diet to 7.5 mEq/day were determined The rGLP-1 significantly attenuated the development of hypertension in Dahl S rats (136 vs. 174 mmHg). This was associated with reduction in proteinuria (46 vs. 128 mg/day) and albuminuria (46 vs. 86 mg/day) and
         Dahl S rats (136 vs. 174 mmHg). This was associated with reduction in proteinuria (46 vs. 128 mg/day) and albuminuria (46 vs. 86 mg/day) and improvement of endothelial function and renal and cardiac damage. The rGLP-1 markedly increased urine flow and sodium excretion for the first 3 days following elevation in sodium intake. It had no significant effects on plasma glucose and insulin conens. The rGLP-1 has antihypertensive and cardiac and renoprotective effects in Dahl S rats fed a high salt diet. The antihypertensive effect of rGLP-1 in
            Dahl S rats is due mainly to its diuretic and natriuretic effects, rather
            RL: BSU (Biological study, unclassified); BIOL (Biological study)
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studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GLP-1 effect on water and sodium excretion in Dahl
salt-sensitive hypertensive rats)

IT 89750-14-1, Glucagon-like peptide 1 118549-37-4, Insulinotropin
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(antihypertensive effect of glucagon-like peptide 1 in Dahl
salt-sensitive rats)

RECNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS
RECORD

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(26) Orskov, C; Diabetes 1994, V47, P815 MEDLINE
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ST hypertension GLP1; sodium water exerction hypertension GLP1; glucose insulin blood hypertension GLP1; aorta heart kidney damage hypertension
   GLP1; albuminuria proteinuria hypertension GLP1; antihypertensive GLP1
    diuresis natriuresis
    Hypertension
(Dahl salt-sensitive; antihypertensive effect of glucagon-like peptide
1 in Dahl salt-sensitive rats)
IT Heart, disease
   Kidney, disease
(GLP-1 effect on aorta endothelium and heart and
       kidney damage in Dahl salt-sensitive hypertensive rats)
IT Blood pressure
   Heart rate
      (GLP-1 effect on blood pressure and heart rate in
Dahl salt-sensitive hypertensive rats)
IT Albumins, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(albuminuria; GLP-1 effect on albuminuria and
      proteinuria in Dahl salt-sensitive hypertensive rats)
IT Antihypertensives
       (antihypertensive action of GLP-1 in Dahl
       salt-sensitive hypertensive rats is due to diuretic and natriuretic
       actions)
     Artery, disease
      (aortic endothelial injury; GLP-1 effect on aorta
endothelium and heart and kidney damage in Dahl salt-sensitive
      hypertensive rats)
      (aortic endothelial; GLP-1 effect on aorta
       endothelium and heart and kidney damage in Dahl salt-sensitive
      hypertensive rats)
      (aortic, disease, injury; GLP-1 effect on aorta endothelium and heart and kidney damage in Dahl salt-sensitive
      hypertensive rats)
   RL: BSU (Biological study, unclassified); BIOL (Biological study) (proteinuria; GLP-1 effect on albuminuria and
proteinuria in Dahl salt-sensitive hypertensive rats)

IT 50-99-7, Glucose, biological studies 9004-10-8, Insulin, biological
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RL: BSU (Biological study, unclassified); BIOL (Biological study)
      (GLP-1 effect on blood glucose and insulin in Dahl salt-sensitive hypertensive rats)
IT 7440-23-5, Sodium, biological studies 7732-18-5, Water, biological
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than an effect to improve insulin-resistance.

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(44) Zou, A; Hypertension 1996, V27, P631 CAPLUS
 => D Ibib ALL 128
 L28 ANSWER I OF I CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:447519 CAPLUS <<LOGINID::20070124>>
DOCUMENT NUMBER: 139:255595
                                 Antihypertensive effect of glucagon-like peptide 1 in
                          Dahl salt-sensitive rats
Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly,
 AUTHOR(S):
                          Annette; Ditter, Katie; Mistry, Mahesh; Roman, Richard
                           SOURCE: Department of Physiology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA
 CORPORATE SOURCE:
                                    Journal of Hypertension (2003), 21(6),
SOURCE:
                           1125-1135
                         CODEN: JOHYD3; ISSN: 0263-6352
 PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AN 2003:447519 CAPLUS <<LOGINID::20070124>>
DN 139:255595
 ED Entered STN: 11 Jun 2003
 TI Antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive
rats
AU Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly, Annette; Ditter,
Katie; Mistry, Mahesh; Roman, Richard J.
CS Department of Physiology, Medical College of Wisconsin, Milwaukee, WI,
     53226, USA
33226, USA
SO Journal of Hypertension (2003), 21(6), 1125-1135
CODEN: JOHYD3; ISSN: 0263-6352
PB Lippincott Williams & Wilkins
DT Journal
        2-6 (Mammalian Hormones)
        Dahl salt-sensitive (Dahl S) rats exhibit many phenotypic traits associated
```

with salt-sensitive hypertension in man. Specifically, they are salt-sensitive, insulin-resistant and hyperlipidemic. They also develop endothelial dysfunction, cardiac injury and glomerulosclerosis. Insulin resistance is linked to hypertension, renal and cardiac damage and endothelial dysfunction. Thus, an agent that has diuretic action and can improve insulin resistance, like recombinant glucagon-like peptide-1(7-36)amide (rGLP-1), may have an antihypertensive effect. To peptide-1(7-36)amide (rGLP-1), may have an antihypertensive effect. To determine whether chronic administration of rGLP-1 attenuates the development of hypertension, endothelial dysfunction and/or hypertension-induced renal and cardiac end organ damage in Dahl S rats. Mean arterial pressure (MAP) and urinary excretion of protein and albumin were measured in Dahl S rats before and after they were fed a 8% NaCl diet and infused with rGLP-1 (1 mg/kg per min, i.v.) or vehicle for 14 days. At the end of the study, the degree of renal and cardiac injury was histol. assessed and endothelium-dependent relaxing function was studied using sortic rings. In other rats, the effects of rGLP-1 on sodium and water balance and lastma places and insulie levels for the first 3 days (following a step). plasma glucose and insulin levels for the first 3 days following a step change in sodium intake from a 0.1% NaCl diet to 7.5 mEq/day were determined change in sodium intake from a 0.1% NaCl diet to 7.5 mEq/day were determ. The rGLP-1 significantly attenuated the development of hypertension in Dahl S rats (136 vs. 174 mmHg). This was associated with reduction in proteinuria (46 vs. 128 mg/day) and allbuminuria (46 vs. 86 mg/day) and improvement of endothelial function and renal and cardiac damage. The rGLP-1 markedly increased urine flow and sodium excretion for the first 3 days following elevation in sodium intake. It had no significant effects on plasma glucose and insulin conens. The rGLP-1 has antihypertensive and cardiac and renoprotective effects in Dahl S rats fed a high salt diet. The antihypertensive effect of rGLP-1 in Dahl S rats fed a bigh salt diet. Dahl S rats is due mainly to its diuretic and natriuretic effects, rather than an effect to improve insulin-resistance.

ST hypertension GLP1; sodium water excretion hypertension GLP1; glucose insulin blood hypertension GLP1; aorta heart kidney damage hypertension GLP1; albuminuria proteinuria hypertension GLP1; antihypertensive GLP1

IT Hypertension

(Dahl salt-sensitive; antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive rats)

IT Heart, disease Kidney, disease

(GLP-1 effect on aorta endothelium and heart and

kidney damage in Dahl salt-sensitive hypertensive rats)

IT Blood pressure

Heart rate (GLP-I effect on blood pressure and heart rate in

Dahl salt-sensitive hypertensive rats)
IT Albumins, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

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L29 ANSWER I OF I CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2003:447519 CAPLUS <<LOGINID::20070124>> DOCUMENT NUMBER: 139:255595 Antihypertensive effect of glucagon-like peptide 1 in

(albuminuria: GLP-1 effect on albuminuria and proteinuria in Dahl salt-sensitive hypertensive rats)
IT Antihypertensives

(antihypertensive action of GLP-1 in Dahl salt-sensitive hypertensive rats is due to diuretic and natriuretic actions)

IT Artery, disease

(aortic endothelial injury; GLP-1 effect on aorta endothelium and heart and kidney damage in Dahl salt-sensitive hypertensive rats)

(aortic endothelial: GLP-1 effect on aorta endothelium and heart and kidney damage in Dahl salt-sensitive hypertensive rats) IT Endothelium

(aortic, disease, injury; GLP-1 effect on aorta endothelium and heart and kidney damage in Dahl salt-sensitive hypertensive rats)

RL: BSU (Biological study, unclassified); BIOL (Biological study) (proteinuria; GLP-1 effect on albuminuria and proteinuria in Dahl salt-sensitive hypertensive rats)

IT 50-99-7, Glucose, biological studies 9004-10-8, Insulin, biological

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(GLP-1 effect on blood glucose and insulin in Dahl salt-sensitive hypertensive rats) IT 7440-23-5, Sodium, biological studies 7732-18-5, Water, biological

RL: BSU (Biological study, unclassified); BIOL (Biological study) (GLP-1 effect on water and sodium exerction in Dahl salt-sensitive hypertensive rats)

IT 89750-14-1, Glucagon-like peptide I 118549-37-4, Insulinotropin RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Lantihypertensive effect of glucagon-like peptide I in Dahl

salt-sensitive rats)

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD

(1) Anderson, S; J Clin Invest 1985, V76, P612 CAPLUS (2) Barragan, J; Am J Physiol 1994, V266, PE459 CAPLUS (3) Bishop, J; Cardiovasc Res 2000, V47, P57 CAPLUS (4) Bullock, B; Endocrinology 1996, V137, P2968 CAPLUS (5) Campese, V; Hypertension 1994, V23, P531 MEDLINE

(6) Dall'Aglio, E; Am J Hypertens 1991, V4, P773 CAPLUS

Dahl salt-sensitive rats
Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly, AUTHOR(S): Annette; Ditter, Katie; Mistry, Mahesh; Roman, Richard

CORPORATE SOURCE: SOURCE: Department of Physiology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA

SOURCE: Journal of Hypertension (2003), 21(6),

1125-1135 CODEN: JOHYD3; ISSN: 0263-6352

Lippincott Williams & Wilkins Journal PUBLISHER:

DOCUMENT TYPE:

LANGUAGE: English
AN 2003:447519 CAPLUS <<LOGINID::20070124>>

DN 139:255595

ED Entered STN: 11 Jun 2003

TI Antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive

AU Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly, Annette; Ditter, Katie; Mistry, Mahesh; Roman, Richard J.
CS Department of Physiology, Medical College of Wisconsin, Milwaukee, WI,

53226, USA SO Journal of Hypertension (2003), 21(6), 1125-1135

CODEN: JOHYD3; ISSN: 0263-6352 PB Lippincott Williams & Wilkins

DT Journal

LA English
CC 2-6 (Mammalian Hormones)

CC 2-6 (Mammalian Hormones)

AB Dahl salt-sensitive (Dahl S) rats exhibit many phenotypic traits associated with salt-sensitive (Dahl S) rats exhibit many phenotypic traits associated with salt-sensitive, hypertension in man. Specifically, they are salt-sensitive, insulin-resistant and hyperlipidemic. They also develop endothelial dysfunction, eardiac injury and glomeruloscrosis. Insulin resistance is linked to hypertension, renal and cardiac damage and endothelial dysfunction. Thus, an agent that has diuretic action and can improve insulin resistance, like recombinant glucagon-like peptide-1(7-36)amide (rGLP-1), may have an antihypertensive effect. To determine whether chronic administration of rGLP-1 attenuates the development determine whether chronic administration of rGLP-1 attenuates the developm of hypertension, endothelial dysfunction and/or hypertension-induced renal and cardiac end organ damage in Dahl S rats. Mean arterial pressure (MAP) and urinary excretion of protein and albumin were measured in Dahl S rats before and after they were fed a 8% NaCl diet and infused with rGLP-1 (1 mg/kg per min, i.v.) or vehicle for 14 days. At the end of the study, the degree of renal and cardiac injury was histol. assessed and endothelium-dependent relaxing function was studied using aortic rings. In other rats, the effects of rGLP-1 on sodium and water balance and plasma glucose and instillin levels for the first 3 days following a step change in sodium intake from a 0.1% NaCl diet to 7.5 mEn/day were determined. change in sodium intake from a 0.1% NaCl diet to 7.5 mEq/day were determined

The rGLP-1 significantly attenuated the development of hypertension in The rGLP-1 significantly attenuated the development of hypertension in Dahl S rats (136 vs. 174 mmHg). This was associated with reduction in proteinuria (46 vs. 128 mg/day) and albuminuria (46 vs. 86 mg/day) and improvement of endothelial function and renal and cardiac damage. The rGLP-1 markedly increased urine flow and sodium excretion for the first 3 days following elevation in sodium intake. It had no significant effects on plasma glucose and insulin conens. The rGLP-1 has antihypertensive and cardiac and renoprotective effects in Dahl S rats fed a high salt diet. The antihypertensive effect of rGLP-1 in Dahl S rats is due mainly to its diversit and particulative effects rather than an effect in improve. diuretic and natriuretic effects, rather than an effect to improve

insulin-resistance.

ST hypertension GLP1; sodium water excretion hypertension GLP1; glucose insulin blood hypertension GLP1; and exert kidney damage hypertension GLP1; albuminuria proteinuria hypertension GLP1; antihypertensive GLP1 diuresis natriuresis

IT Hypertension

(Dahl salt-sensitive; antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive rats)

IT Heart, disease

Kidney, disease
(GLP-1 effect on aorta endothelium and heart and kidney damage in Dahl salt-sensitive hypertensive rats)
IT Blood pressure

(GLP-1 effect on blood pressure and heart rate in

Oahl salt-sensitive hypertensive rats)
Albumins, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(albuminuria; GLP-1 effect on albuminuria and
proteinuria in Dahl salt-sensitive hypertensive rats)

IT Antihypertensives

(antihypertensive action of GLP-1 in Dahl

salt-sensitive hypertensive rats is due to diuretic and natriuretic actions)

IT Artery, disease
(aortic endothelial injury; GLP-1 effect on aorta

endothelium and heart and kidney damage in Dahl salt-sensitive hypertensive rats)

Injury (aortic endothelial; GLP-1 effect on aorta

endothelium and heart and kidney damage in Dahl salt-sensitive hypertensive rats)

Endothelium

(aortic, disease, injury; GLP-1 effect on aorta endothelium and heart and kidney damage in Dahl salt-sensitive

hypertensive rats)

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L30 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN 2003:447519 CAPLUS <<LOGINID::20070124>> 139:255595 ACCESSION NUMBER:

DOCUMENT NUMBER:

Antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive rats

AUTHOR(S):

Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly, Annette; Ditter, Katie; Mistry, Mahesh; Roman, Richard

SOURCE: Department of Physiology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA CORPORATE SOURCE:

SOURCE: Journal of Hypertension (2003), 21(6), 1125-1135

CODEN: JOHYD3; ISSN: 0263-6352 Lippincott Williams & Wilkins

PUBLISHER: DOCUMENT TYPE: Journal

LANGUAGE: English
REFERENCE COUNT: 44 44 THERE ARE 44 CITED REFERENCES

AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D Ibib All L33 1-9

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IT Proteins
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RL: BSU (Biological study, unclassified); BIOL (Biological study) (proteinuria; GLP-1 effect on albuminuria

and proteinuria in Dahl salt-sensitive hypertensive rats)

IT 50-99-7, Glucose, biological studies 9004-10-8, Insulin, biological

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GLP-1 effect on blood glucose and insulin in Dahl
salt-sensitive hypertensive rats)

IT 7440-23-5, Sodium, biological studies 7732-18-5, Water, biological

studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (GLP-1 effect on water and sodium excretion in Dahl salt-sensitive hypertensive rats)

17 89750-14-1, Glucagon-like peptide 1 118549-37-4, Insulinotropin
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antihypertensive effect of glucagon-like peptide 1 in Dahl

salt-sensitive rats)
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS

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(1) Anderson, S; J Clin Invest 1985, V76, P612 CAPLUS

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(1) Anderson, S; J Clin Invest 1985, V76, P612 CAPLUS
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L33 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2004:533962 CAPLUS <<LOGINID::20070124>>

DOCUMENT NUMBER: 141:82335 Human glucagon-like-peptide-1 mimics and their

antidiahetic effects

INVENTOR(S):): Natarajan, Sesha Iyer, Mapelli, Claudio; Bastos, Margarita M.; Bernatowicz, Michael; Lee, Ving; Ewing,

Margaria M.; Bernatowicz, Michael; Lee, Ving; Ewing, William R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat Appl. Publ., 73 pp., Cont.-in-part of U.S.
CODEN: USXXCO

DOCUMENT TYPE: LANGUAGE: English FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

US 2003-419399 US 2002-273975 US 2003195157 A1 20031016 20021018 <--A2 20041104 A3 20050915 WO 2004-US12374 WO 2004094461

VO 2004094461 A3 20050915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BR, BI, CF, CG, LC M, GA, GN, GO, GW, ML, MR, NE, SN.

ED Entered STN: 02 Jul 2004

TI Human glucagon-like-peptide-I mimics and their antidiabetic effects IN Natarajan, Sesha lyer, Mapelli, Claudio; Bastos, Margarita M.;

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PA USA
SO U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 273,975.
           CODEN: USXXCO
 DT Patent
 LA English
IC ICM A61K038-10
ICS C07K007-08
  INCL 514015000; 530328000
 CC 1-10 (Pharmacology)
Section cross-reference(s): 2, 34, 63
FAN.CNT 2
            PATENT NO.
                                                                                            KIND DATE
                                                                                                                                                                       APPLICATION NO.
                                                                                            A1 20040701 US 2003-419399
A1 20031016 US 2002-273975
A2 20041104 WO 2004-US12374
A3 20050915
 PI US 2004127423
                                                                                                                                                                                                                                                              20030421
                                                                                                                                                                                                                                                          20021018
              WO 2004094461
                                                                                                                                                                                                                                                                      20040421
                     /O 2004094461 A3 20050915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CL, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
            TD, TG
EP 1615653
                                                                                       A2 20060118 EP.2004-760098
                       R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
          E. 31, E. 74, E.
 PRAI US 2001-342015P
 CLASS
   PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES
 US 2004127423 ICM A61K038-10
ICS C07K007-08
INCL 514015000; 530328000
IPCI A61K0038-10 [ICM,7]; C07K0007-08 [ICS,7]; C07K0007-00
                                          [ICS,7,C*]
IPCR A61K0038-00 [N,C*]; A61K0038-00 [N,A]; C07K0014-435
                                                        [1,C*]; C07K0014-605 [1,A]
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Bernatowicz, Michael; Lee, Ving; Ewing, William R.

(MTP (microsomal triglyceride-exchanging protein), inhibitors; human glucagon-like-peptide-1 mimics and their antidiabetic effects) Antiarteriosclerotics (antiatherosclerotics; human glucagon-like-peptide-1 mimics and their antidiahetic effects) Drug delivery systems (capsules; human glucagon-like-peptide-1 mimics and their antidiabetic effects) RL: BSU (Biological study, unclassified); BIOL (Biological study) (cholesterol ester-exchanging; human glucagon-like-peptide-1 mimics and their antidiabetic effects) Kidney, disease (diabetic nephropathy; human glucagon-like-peptide-1 mimics and their antidiabetic effects) Nerve, disease (diabetic neuropathy; human glucagon-like-peptide-1 mimics and their antidiabetic effects) IT Eye, disease
(diabetic retinopathy; human glucagon-like-peptide-1 mimics and their (unabelet tempany), minima gridagon-ince-peptide-i minima and uteri antidiabetic effects). IT Transport proteins RL BSU (Biological study, unclassified); BIOL (Biological study) (dopamine transporter; human glucagon-like-peptide-i mimics and their antidiabetic effects) IT 5-HT reuptake inhibitors Antihypertensives Antiobesity agents Appetite depressants Atherosclerosis Diabetes mellitus Human Hyperglycemia Hypertension Hypertriglyceridemia Hypolipemic agents Obesity Signal transduction, biological Wound healing b3-Adrenoceptor agonists (human glucagon-like-peptide-1 mimics and their antidiabetic effects)
IT Fatty acids, biological studies Glucagon-like peptide-1 receptors Hyperlipidemia Thyroid hormone receptors RL: BSU (Biological study, unclassified); BIOL (Biological study)

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NCL 514/015.000; 530/328.000
ECLA CO7K014/605
US 2003195157 PCI A61K0038-10 [ICM,7]; A61K0038-08 [ICS,7]; C07K0007-08 [ICS,7]; C07K0007-06 [ICS,7]; C07K0007-06 [ICS,7]; C07K0007-06 [ICS,7]; C07K0007-06 [ICS,7]; C07K0007-08 [ICS,7]; C07K0007-06 [ICS,7]; C07K0007-08 [ICS,7]; C07K0014-05 [ICS,7]; C07K0014-05 [IA]
NCL 514/016.000; 514/017.000; 530/328.000; 530/329.000
ECLA C07K014/600
WO 2004099461 PCI C07K [ICM,7]
IPCR A61K0038-02 [IA]; A61K0038-06 [IA]; A61K0038-02 [IC*]; A61K0038-02 [IA]; A61K0038-01 [IC*]; A61K0038-02 [IA]; A61K0038-00 [IA]; A61K0038-01 [IA]; C07K007-04 [IA]; C07K007-09 [IA]
EP 1615653 PCI A61K0038-08 [ICS,7]; A61K0038-02 [ICS,7]; A61K0038-01 [ICS,7]; A61K0038-08 [ICS,7]; C07K0007-04 [ICS,7]; C07K0007-04 [ICS,7]; C07K0007-06 [ICS,7]; C07K
CO7K0007-04 [ICS,7]; CO7K0007-08 [ICS,7]; CO7K0007-00 [ICS,7,6]]

IPCR A61K0038-00 [I,C*]; A61K0038-00 [I,A]; A61K0038-02 [I,C*]; A61K0038-02 [I,A]; A61K0038-08 [I,C*]; A61K0038-02 [I,A]; A61K0038-08 [I,C*]; A61K0038-08 [I,C*]; A61K0038-10 [I,C*]; A61K0038-10 [I,C*]; CO7K0007-02 [I,A]; CO7K0007-04 [I,A]; CO7K0007-08 [I,A]

AB The invention discloses human glucagon-like peptide-1 (GIP-1) peptide mirnies that mirnic the biol. activity of the native
        GLP-I peptide and thus are useful for the treatment or
prevention of diseases or disorders associated with GLP activity. Further,
        prevention of diseases or disorders associated with GLP activity. Furth
the invention provides novel, chemical modified peptides that not only
stimulate insulin secretion in type II diabetics, but also produce other
beneficial insulinotropic responses. These synthetic peptide GLP
-1 mimites exhibit increased stability to proteolytic cleavage
making them ideal therapeutic candidates for oral or parenteral
          administration.
 ST human glucagon peptide mimic prepn diabetes antidiabetic insulin stability
          RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
        (Biological study); USES (Uses)
(ALBP (adipocyte lipid-binding protein); human glucagon-like-peptide-I
               mimics and their antidiabetic effects)
               ipoprotein receptors
        RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LDL; human glucagon-like-peptide-1 mimics and their antidiabetic
              effects)
         RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
        (Biological study); USES (Uses)
(human glucagon-like-peptide-1 mimics and their antidiabetic effects)
IT Peptides, biological studies
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
         (Uses)
             (human glucagon-like-peptide-1 mimics and their antidiabetic effects)
IT Sulfonylureas
        RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
        (Biological study); USES (Uses)
(human glucagon-like-peptide-1 mimics and their antidiabetic effects)
           Drug delivery systems
             (injections; human glucagon-like-peptide-1 mimics and their antidiabetic effects)
 IT Metabolic disorders
              (metabolic syndrome X; human glucagon-like-peptide-1 mimics and their
              antidiabetic effects)
           Drug delivery systems
             (microparticles; human glucagon-like-peptide-1 mimics and their
                antidiabetic effects)
IT Diabetes mellitus
             (non-insulin-dependent; human glucagon-like-peptide-1 mimics and their antidiabetic effects)
 IT Antidiabetic agents
        Drug delivery systems
             (oral; human glucagon-like-peptide-1 mimics and their antidiabetic
IT Drug delivery systems
             (suspensions; human glucagon-like-peptide-1 mimics and their
              antidiabetic effects)
          Drug delivery syste
                     blets; human glucagon-like-peptide-1 mimics and their antidiabetic
              effects)
 TP Peroxisome proliferator-activated receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(a; human glucagon-like-peptide-1 mimics and their antidiabetic
              effects)
TT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(g; human glucagon-like-peptide-1 mimics and their antidiabetic
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T 51-61-6, Doparnine, biological studies 56-81-5, Glycerol, biological studies 9001-62-1, Lipase 9028-35-7, 3-Hydroxy-3-methylglutaryl CoA reductase 9029-60-1, Lipoxygenase 9033-06-1, Glucosidase 9077-14-9, Squalene synthetase 63551-74-6, Lipoxygenase 90002-36-1, 2-Ethylphenyl

RL: BSU (Biological study, unclassified); BIOL (Biological study)

NCL 514/015.000: 530/328.000

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(human glucagon-like-peptide-1 mimics and their antidiabetic effects)

IT $16514-32-2P $16514-38-8P $16514-43-5P $16514-47-9P $16514-68-4P $16514-75-3P $16514-75-3P $16514-75-3P $16514-47-9P $16514-68-4P $16514-78-7P $16514-19-3P $16514-95-7P $16514-64-0P $16515-00-6P $16515-06-3P $16515-06-3P $16515-00-6P $16515-14-3P $16515-14-3P $16515-10-30-P $16515-20-3P $16515-26-3P $16515-20-3P $16515-34-7P $16515-30-3P $16515-34-7P $16515-34-7P $16515-52-P $16515-68-1P $16515-52-7P $16515-55-2P $16515-58-1P $16515-52-7P $16515-58-1P $16515-68-64-P $16515-68-64-P $16516-14-6P $16516-14-6P $16516-16-40-P $16516-64-6P $16516-62-P $16516-64-6P $16516-63-6P $16516-50-0P $16516-63-5P $16516-63-6P $16516-64-P $16516-64-P $16516-63-PP $16516-50-0P $16516-35-1P $16516-63-PP $16516-50-0P $16517-33-PP $16518-30-2P $16519-30-3P $16520-30-3P $16520-30-3P $16520-30-3P $16520-30-3P $16520-30-3P $16520-30-3P $16520-30-3P $16520-30-3P $1652
                         516521-42-9P 516521-43-0P 516521-44-1P 516521-45-2P 516521-53-2P
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RL: SPN (Synthetic preparation); PREP (Preparation)
(human glucagon-like-peptide-1 mimics and their antidiabetic effects) IT 9027-63-8, ACAT
   SUC Biological study, unclassified); BIOL (Biological study) (inhibitors; human glucagon-like-peptide-1 mimics and their antidiabetic effects)
IT 54249-88-6, Dipeptidyl peptidase IV
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(inhibitors; human glucagon-like-peptide-1 mimics and their
antidiabetic effects)

IT 9004-10-8, Insulin, biological studies
   RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance, hyperinsulinemia; human glucagon-like-peptide-1 mimics and
       their antidiabetic effects)
L33 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:157498 CAPLUS <<LOGINID::20070124>>
DOCUMENT NUMBER: 140:199313
TITLE: Preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors
INVENTOR(S): Daisy, Joe
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 71 pp.
CODEN: EPXXDW
DOCUMENT TYPE.
DOCUMENT TYPE:
                                      Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:
                                 English
    PATENT NO.
                                KIND DATE APPLICATION NO.
                                                                                                  DATE
    EP 1391460
                               A1 20040225 EP 2003-20676
                                                                                        20000918
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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    EP 1088824
                              A2 20010404 EP 2000-308131
                                                                                        20000918 <--
                               A3 20010627
    EP 1088824
                               B1 20040107
       R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
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A1 20021205 US 2002-117370 B2 20030610

EP 2000-308131 A3 20000918

20030214 <--

US 1999-157148P P 19990930

US 2003195361 A1 20031016 US 2003-367002 US 6828343 B2 20041207 PRIORITY APPLN. INFO:: US 1999-157148P

US 2002183369

US 6576653

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preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

    (Preparation); USES (USES)
    (human glucagon-like-peptide-1 mimics and their antidiabetic effects)
    713497-79-1P 713497-81-5P 713497-83-7P 713497-85-9P
    RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (human glucagon-like-peptide-1 mimics and their antidiabetic effects)

IT 51-64-9, Dexamphet-amine 56-03-1, Biguanide 94-20-2, Chloropropamide 122-09-8, Phentermine 637-07-0, Clofibrate 657-24-9, Metformin 943-45-3D, Fibric acid, derivs. 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 21187-98-4, Gliclazide 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 56180-94-0, Acarbose 72432-03-2, Miglitol 75330-75-5, Lovastatin 7902-63-9, Simvastatin 81093-37-0, Pravastatin 89750-14-1, Glucagon-like peptide 1 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 122320-73-4, Resiglitazone 134523-00-5, Ator-vastatin 15062-02-1, Repaglinide 141750-63-2, Nisvastatin 141758-49-9, AC2993 144288-97-1, TS-962 145599-86-6, Cerivastatin 152755-31-2, LY295427 159183-92-3, L750355 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 170861-63-9, TIT-501 176435-10-2, LY3115902 178759-95-0, MD 700 196808-45-4 199113-98-9, NN-2344 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, Al9677 258345-41-4, GW-409544 262352-17-0, CP 529414 282526-693, ATL-962 287714-41-4 335149-08-1, L896454 335149-14-9, R-119702 335149-15-0, KAD1129 335149-17-2, AR-H039242 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipyride 444069-80-1, Axokine RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (bitongical study); OSES (USES)
(human glucagon-like-peptide-1 mimics and their antidiabetic effects)
IT 150-46-9, Triethylborate 358-23-6, Triflic anhydride 1973-22-4,
1-Bromo-2-ethylbonzene 4326-36-7 16419-60-6, O-Tolylboronic acid
82911-69-1 93267-04-0 516521-49-6 713497-86-0
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(human glucagon-like-peptide-1 mimics and their antidiabetic effects)

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IT 713497-87-1P 713497-88-2P
                                                                          US 2000-670759 A3 20000927
US 2002-117370 A3 20020405
 US 2002-117370 A3 20020
OTHER SOURCE(S): MARPAT 140:199313
AN 2004:157498 CAPLUS <<LOGINID::20070124>>
DN 140:199313
ED Finiand STR.
   ED Entered STN: 26 Feb 2004
  T1 Preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors
  IN Daisy, Joe
PA Pfizer Products Inc., USA
  SO Eur. Pat. Appl., 71 pp.
CODEN: EPXXDW
   DT Patent
  LA English
IC ICM C07D495-04
         ICS C07D491-04; C07D209-52; A61K031-407; A61P003-10; A61P009-10; C07D495-14; C07D333-00; C07D209-00; C07D307-00
   CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
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               EP 1391460 A1 20040225 EP 2003-20676 20000918
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EP 1088824
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                                                            A3 20010627
B1 20040107
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A61P009-10; C07D495-14; C07D333-00; C07D209-00;
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C07D307-00

IPCI C07D0495-04 [ICM,7]; C07D0491-04 [ICS,7]; C07D0491-00

516521-54-3P 516521-55-4P 713497-71-3P 713497-72-4P 713497-73-5P 713497-74-6P 713497-75-7P 713497-77-9P RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic

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[ICS,7,C*]; C07D0209-52 [ICS,7]; A61K0031-407 [ICS,7]; A61P0003-10 [ICS,7]; A61P0003-00 [ICS,7,C*]; A61P0009-10 [ICS,7,C*]; C07D0495-01 [ICS,7,C*]; C07D0495-01 [ICS,7,C*]; C07D0495-00 [ICS,7,C*]; C07D0495-00 [ICS,7,C*]; C07D0495-00 [ICS,7,C*]; C07D0495-00 [ICS,7,C*]; C07D0495-00 [ICS,7]; C07D0307-00
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                                                                                                                    [ICS,7]
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[ICS,6]; A61K0031-407 [ICS,6]; A61P0009-10 [ICS,6];
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A61P0003-10 [I,C*]; A61P0003-10 [I,A];
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A61P0009-01 [I,A]; A61P003-00 [I,A];
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[I,C*]; CO7F0007-10 [LA]; CU/KUU03-00 [LC-];
CO7K0005-00 [LA]
ECLA CO7D209/52; CO7D491/04+307B+209B; CO7D495/04+333B+209B
US 2002183369 PCI CO7D0513-22 [ICM,7]; CO7D0513-00 [ICM,7,C*];
A61K0031-429 [ICS,7]; A61K0031-424 [ICS,7];
A61K0031-4188 [ICS,7]; A61K0031-4164 [ICS,7,C*]
IPCR CO7D0209-00 [LC*]; CO7D0209-52 [LA]; CO7D0491-00
[I,C*]; CO7D0491-04 [LA]; CO7D0495-00 [I,C*];
CO7TD0405-04 II A1
[I,C*]; C07D0491-04 [I,A]; C07D0495-00 [I,C*];
C07D0495-04 [I,A]
NCL 514/367.000; 514/375.000; 514/393.000; 514/412.000;
548/153.000; 548/217.000; 548/303.100; 548/453.000
ECLA C07D090/52; C07D0491/04+307B±209B; C07D0495/04+333B+209B
US 2003195361 IPCI C07D0513-12 [ICM,7]; C07D0498-02 [ICS,7]; C07D0498-00
[ICS,7,C*]; C07D0613-02 [ICS,7]; C07D0413-00
[ICS,7,C*]; C07D047-02 [ICS,7]; C07D0498-00 [ICS,7,C*]
IPCR C07D0209-00 [I,C*]; C07D0495-00 [I,C*]; C07D0491-00
[I,C*]; C07D0491-04 [I,A]; C07D0495-00 [I,C*]; C07D0495-04 [I,A]; C07D0495-04 [I,A]; C07D0495-04 [I,A]; C07D0495-04 [I,A]; C07D0495-00 [I,C*]; C07D0495-04 [I,A]; C07D0495-00 [I,C*]; C07D0495-04 [I,A]; C07D0495-00 [I,C*]; C07D0495-04 [I,A]; C07D0495-00 [I,C*]; C07D0495-04 [I,A]; C07D0495-04
                                                                                                                                                                                 C07D0495-04 [LA]
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```
(diabetic nephropathy, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
     Nerve, disease
(diabetic neuropathy, treatment; preparation of fused pyrrolylcarboxamides
        as glycogen phosphorylase inhibitors)
      Eye, disease
       (diabetic retinopathy, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
IT Antioxidants
       (fatty acid oxidation inhibitors coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
IT Gluconeogenesis
       (inhibitors coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
       (ischemia, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
IT Anti-ischemic agents
     Anticholesteremic agents
     Antidiabetic agents
     Antihypertensives
Drug delivery systems
     Human
     Hypolipemic agents
        (preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
IT Atherosclerosis
     Cataract
     Diabetes mellitus
     Hypercholesterolemia
     Hyperglycemia
      Hypertriglyceridemi
     Ischemia
       (treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
IT Hyperlinidemia
    RL: BSU (Biological study, unclassified); BIOL (Biological study) (treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

    Peroxisone proliferator-activated receptors
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
    (g. PPAR-g agonists coadministration; preparation of fused
    pytrolylearboxamides as glycogen phosphorylase inhibitors)
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phosphorylase inhibitors)

1T Kidney, disease

NCL 548/153.000; 548/218.000; 548/303.100; 548/453.000 ECLA C07D209/52; C07D491/04+307B+209B; C07D495/04+333B+209B OS MARPAT 140:199313

AB Title compds. [I; Q = substituted aryl, heteroaryl; Z, X = C, CH, CH2, N, O, S; X1 = NRa, CH2, O, S; dotted lines = bond, null; both dotted lines are not simultaneously bonds; R1 = H, halo, alkoxy, alkythio, alkyl, CF3, NH2, alkylamino, dialkylamino, NO2, CN, CO2H, carboxyalkyl, alkenyl, alkenyl, alkynyl; Ra, Rb = H, alkyl; Y = CH(OH), null; R2R3 = atoms to form a 5-6 membered ring containing O-3 heteroatoms and 0-2 double bonds; R4 = COA; A = NRdRd, NRaCH2CH2ORa, N-heterocycly!; Rd = H, alkyl, alkoxy, aryl, (substituted) aryl, heteroaryl; Rc = H, CO2Ra, ORa, SRa, NRaRa; n = 1-3], were prepared for treatment of diabetes, insulin resistance, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, cataracts, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, altherosclerosis, or tissue ischemia (no data). Thus, 6H-thieno[2,3-b]pyrrole-5-carboxylic acid and (3S)-amino-1-((3R,4S)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-4-phenylbutan-1-one were coupled using 4-(dimethylamino)pyridine, 1-hydroxybenzotriazole hydrate and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in CH2C12/DMF to give 6H-thieno[2,3-b]pyrrole-5-carboxylic acid ((1S)-benzyl-3-((3R,8S)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-3-oxopropyl]amide.

(Naschania nephropathy retinopathy cataract hyperglycernia hypercholesterolemia hypertension treatment pyrrolecarboxamide; hyperinsulinemia hypertipidemia atherosclerosis tissue ischemia treatment fused pyrrolecarboxamide

(cardiac, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

IT Antiobesity agents a2-Adrenoceptor antagonists

b-Adrenoceptor agonists (coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

Sulfonylureas
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministration; preparation of fused pyrrolylcarboxamides as glycogen

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IT 9007-92-5, Glucagon, biological studies 106602-62-4, Amylin
    RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonists coadministration; preparation of fused pyrrolylearbog glycogen phosphorylase inhibitors)
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(antagonists coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
IT 56-03-1D, Biguanide, derivs. 64-77-7, Tolbutamide 94-20-2,
Chloropropamide 114-86-3, Phenformin 458-24-2, Fenfluramine
657-24-9, Metformin 692-13-7, Buformin 968-81-0, Acetohexamide
1156-19-0, Tolazamide 2295-31-0D, Thiazolidinedione, derivs.
7440-62-2D, Vanadium, complexes 9004-10-8, Insulin, biological studies
9004-10-8D, Insulin, analogs 10238-21-8, Glibenclamide 12179-36-1D,
Pervanadyl (VO(O2)+), complexes 23602-78-0, Benfluorex 28299-33-4D,
Imidazoline, derivs. 29094-61-9, Glipizide 37353-31-4, Vanadate
51037-30-0, Acipimox 51110-01-1D, Somatostatin, analogs 54870-28-9,
Meglitinide 56180-94-0, Acarbose 66529-17-7, Midaglizole 72432-03-2,
Miglitol 74772-77-3, Ciglitazone 75358-37-1, Linogliride 79944-78-4,
Idazoxan 80879-63-6, Emiglitate 84880-29-9, Voglibose 86615-96-5,
BRL35135 88431-47-4, Clomoxir 89197-32-0, Efaroxan 90505-66-1, Ro
16-8714 90730-96-4, BRL37344 93479-97-1, Glimepiride 97322-87-7,
Troglitazone 104343-33-1, MDL-25637 105182-45-4, Fluparoxan
105816-04-4, Nateglinide 106612-94-6, Human GLP-1
(7-37) 107444-51-9, Rat GLP-1(7-36)amide 109229-58-5, Englitazone
110605-64-6, Isaglidole 111023-46-8, Fioglitazone 115656-32-1, D 7114
122320-73-4, Rosiglitazone 122575-28-4, Naglivan 122830-14-2,
Deriglidole 124083-20-1, Etomoxir 172114-23-7, Camiglibose
130714-47-5, WAG 994 133107-64-9, Insulin lispro 135062-02-1,
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141758-74-9, AC2993 187887-46-3, Symlin 395214-16-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of fused pyrrolylcarboxamides as glycogen
phosphorylase inhibitors) (coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

Proceptory as a minimum of process of the proc

(inhibitors coadministration; preparation of tused pyrrolyicarboxai glycogen phosphorylase inhibitors)

IT 9035-74-9, Glycogen phosphorylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

TT 332098-11-0P 332098-12-1P 332098-13-2P 332098-14-3P 332098-15-4P 332098-16-5P 332098-17-6P 332098-18-7P 332098-19-8P 332098-20-1P 332098-21-2P 332098-21-3P 332098-23-4P 332098-20-6P 332098-25-6P 332098-27-8P 332098-28-9P 332098-29-0P 332098-30-3P 332098-31-4P 332098-32-5P 332098-33-6P 332098-34-7P 332098-35-8P 332098-36-9P 332098-37-0P 332098-38-1P 332098-39-2P 332098-40-5P 332098-41-6P 332098-42-7P 332098-43-8P 332098-44-9P 332098-45-0P 332098-46-1P 332098-47-2P 332098-48-3P 332098-49-4P 332098-50-7P

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332098-52-9P 332098-63-2P 332098-55-2P 332098-57-4P 332098-59-6P 332098-61-0P 332098-63-2P 332098-65-4P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

IT 637-81-0, Azidoacetic acid ethyl ester 1066-54-2, (Trimethylsilyl)acetylene 1126-09-6, Piperidine-4-carboxylic acid ethyl ester 4530-18-1, Boc-DL-Phenylalanine 6030-36-0, 4-Methylthiophene-2-carboxaldehyde 7283-96-7, 5-Chlorothiophene-2-carboxaldehyde 13679-70-4, 5-Methyl-2-thiophenecarboxaldehyde 13734-34-4, Boc-L-Phenylalanine 14345-97-2, 2-Chloro-3-methylthiophene 17186-57-1 18791-78-8, 4-Bromothiophene-2-carboxaldehyde 21508-19-0, 5-Chlorofuran-2-carboxaldehyde 21921-76-6, 4-Bromo-2-furaldehyde 24445-35-0 29669-49-6, 5-Fluorothiophene-2-carboxaldehyde 31486-85-8, Thieno[2,3-b]hitophene-2-carboxaldehyde 31486-85-8, Thieno[2,3-b]hitophene-2-carboxaldehyde 31486-85-8, Thieno[2,3-b]hitophene-2-carboxylic acid ethyl ester 39793-31-2, 4H-Thieno[3,2-b]pyrrole-5-carboxylic acid ethyl ester 57500-51-3, 4-Chlorothiophene-2-carboxaldehyde 58963-45-4, 2-Formyl-6H-thieno[2,3-b]pyrrole-5-carboxylic acid ethyl ester 57500-51-3, 4-Chlorothiophene-2-carboxylic acid ethyl ester 5700-51-3, 4-Chlorothiophene-2-carboxylic acid ethyl ester 91545-55-0, 2-Formyl-6H-thieno[2,3-b]pyrrole-5-carboxylic acid ethyl ester 5709-80-4, 2-Formyl-6H-thieno[2,3-b]pyrrole-5-carboxylic acid ethyl ester 91545-55-0, 2-Bromo-6H-thieno[2,3-b]pyrrole-5-carboxylic acid ethyl ester 105181-72-4, (2R.35)3-tert-Butoxycarbonylamino-2-hydroxy-4-phenylbutyric acid 80709-80-4, 2-Rethyl-4H-furo[3,2-b]pyrrole-5-carboxylic acid ethyl ester 105181-72-4, (2R.35)3-tert-Butoxycarbonylamino-2-hydroxy-4-phenylbutyric acid 80709-80-3, 2-Bromo-6H-thieno[3,3-b]pyrrole-5-carboxylic acid ethyl ester 519188-80-8
RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of fused pyrrolyclamboxamides as glycogen phosphorylase inhibitors)

IT 6578
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DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

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PATENT NO.
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            WO 2003059372
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                                                                                                                          WO 2002-DK888
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AU 2002351753 A1 20030730 AU 2002-351753 20021220 <--
EP 1461070 A2 20040929 EP 2002-787467 20021220

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JP 2005516968 T 20050609 JP 2003-559533 20021220

DK 2001-969 A 20011229

US 2002-350087P P 20020117

WO 2002-1969 A 20011229

US 2002-350087P P 20020117

WO 2002-50888 W 20021220

AN 2003:570833 CAPUS <<-li>CAPUS SEN BENEFATIN 36 Id 1003
 DN 139:111682
ED Entered STN: 25 Jul 2003
 TI Combined use of a GLP-1 compound and a modulator of diabetic late complications
IN Knudsen, Lotte Bjerre; Selmer, Johan PA Novo Nordisk A/S, Den. SO PCT Int. Appl., 22 pp. CODEN: PIXXD2
  DT Patent
 LA English
IC ICM A61K038-00
 CC 1-10 (Pharmacology)
Section cross-reference(s): 2, 63
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          PATENT NO.
                                                                   KIND DATE
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US 2003/44206 PC1 A61K0031-26 [ICM-7]; A61K0031-401 [ICS.7]
PCR A61K0031-401 [I,C*]; A61K0031-401 [I,A]; A61K0038-26
[I,C*]; A61K0038-26 [LA]
NCL 514/012.000; 514/423.000
AB Methods and uses for treatment of diabetic late complications comprising administration of a GLP-1 compound and a modulator of diabetic complications.
       diabetic complications.
 ST GLP1 diabetes late complication therapy; glucagon like peptide I analog fragment antidiabetic
 IT Angiotensin receptor antagonists
       Antihypertensives
       Human
       Hypertension
       Protein sequences
       b-Adrenoceptor antagonists
      b1-Adrenoceptor antagonists
(combined use of a GLP-1 compound and a modulate
           diabetic late complications)
        Kidney, disease
          (diabetic nephropathy; combined use of a GLP-
            compound and a modulator of diabetic late complications)
       Nerve, disease
          (diabetic neuropathy; combined use of a GLP-1 compound and a modulator of diabetic late complications)
        Eve. disease
           (diabetic retinopathy; combined use of a GLP-1
           compound and a modulator of diabetic late complications)
 IT Gene, animal
      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (glp-1; combined use of a GLP-1
                mpound and a modulator of diabetic late complications)
          (non-insulin-dependent; combined use of a GLP-1
              ompound and a modulator of diabetic late complications)
 IT Antidiabetic agents
       Drug delivery systems
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4C086/MA04; 4C086/MA07; 4C086/MA52; 4C086/MA55;
                               (oral; combined use of a GLP-1 compound and a
modulator of diabetic late complications)
                       Drug delivery systems
(parenterals; combined use of a GLP-1 compound and a
modulator of diabetic late complications)
496765-91-4
modulator of capetic rate complications)

If 495765-91-4

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
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(combined use of a GLP-1 compound and a modulator of diabetic late complications)
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     L33 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:320036 CAPLUS <<LOGINID::20070124>>
DOCUMENT NUMBER: 138:338498
                                                                                      Preparation of human glucagon-like-peptide-1 mimics
and their use in the treatment of diabetes and related
     INVENTOR(S):
                                                                                                                              Natarajan, Sesha I.; Bastos, Margarita M.;
   Bernatowicz, Michael S.; Mapelli, Claudio, Lee, Ving;
Ewing, William R.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 153 pp.
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CODEN: PIXXD2

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English

DOCUMENT TYPE:

LANGUAGE:

FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. A2 20030424 WO 2002-US33386 A3 20051229 WO 2003033671 20021018 <--WO 2003033671 A2 20030424 WO 2002-US33386 20021018 <-WO 2003033671 A3 20051229

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ZA 2004002846 A 20050816 ZA 2004-2846 20040415

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WO 2002-US313386 W 20021018

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NITHER SOURCE(S): MARPAT 138:338498

NITHER SOURCE(S): MARPAT 138:338498 PRIORITY APPLN. INFO.: WU 2002-US33386 W 200 OTHER SOURCE(S): MARPAT 138:338498 AN 2003:320036 CAPLUS <<LOGINID::20070124>> ED Entered STN: 25 Apr 2003 T1 Preparation of human glucagon-like-peptide-1 mimics and their use in the treatment of diabetes and related conditions IN Natarajan, Sesha I; Bastos, Margarita M.; Bernatowicz, Michael S.; Mapelli, Claudio; Lee, Ving; Ewing, William R. PA Bristol-Myers Squibb Company, USA SO PCT Int. Appl., 153 pp. CODEN: PIXXD2 DT Patent LA English
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CC 34-3 (Amino Acids, Peptides, and Proteins) Section cross-reference(s): 1, 63 FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE

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CLASS

PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

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[N,A]; C07K0014-605 [LA]

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A61P0017-00 [LC*]; A61P0017-02 [LA]; A61P0043-00

[LA]; C07K0014-435 [LC*]; C07K0014-435 [LC*]; A61P0033-00

[NA]; C07K0014-405 [LA]

ECLA C07K014/605

ZA 2004002846 IPCR A61K0038-00 [N,C*]; C07K0014-435 [LC*]; A61K0038-00

[NA]; C07K0014-605 [LA]

ECLA C07K014/605

ZA 2004002846 IPCR A61K0038-00 [N,C*]; C07K0014-435 [LC*]; A61F0038-00

[NA]; C07K0014-605 [LA]

ECLA C7K014/605

ZA 2004002846 IPCR A61K0038-00 [N,C*]; C07K0014-405 [LA]

ECLA C7K014/605

ZA 2004002846 IPCR A61K0038-00 [N,C*]; C07K0014-405 [LA]

ECLA C7K0114-605 [LA]

ECLA C7K0114/605
```

1-15 amino acid residues, an R group [H, (cyclo)alkyl, cycloalkylalkyl, heterocyclyl, heterocycloalkyl, (heterolaryl, arylalkyl, aryloxyalkyl, heteroarylalkyl, or heteroaryloxyalkyl], an RCO (amide) group, a carbamate group, a urea, a sulfonamido, or an aminosulfonyl group; B is OH, alkoxy, etc., an amino or amino acid residue, or a peptide containing from 1-15 amino acid residues, terminating at the C-terminus as a carboxamide, ester, carboxyl, or an amino alc.] that mimic the biol. activity of the native carooxy, or an amino aic.] that minic the oils activity of the native GLP-1 peptide and thus are useful for the treatment or prevention of diseases or disorders associated with GLP activity. These chemical-modified peptides stimulate insulin secretion in type II diabetics and produce other beneficial insulinotropic responses, while exhibiting and produce other beneficial insulinotropic responses, while exhibiting increased stability to proteolytic cleavage making them ideal therapeutic candidates for oral or parenteral administration. A method of preparing the polypeptides comprises replacing the message sequence of the polypeptide with a variant message sequence capable of inducing receptor mediated signal transduction. An example is claimed peptide H-AEGTFTSD-Bip(2-Et)-Bip(2-Me)-NH2 (Bip = biphenylalanine residue).

ST glucagon like peptide minic prepn treatment diabetes

IT Antiarteriosclerotics

(antiatherosclerotics; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

IT Kidney, disease

(diabetic nephropathy; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

Nerve, disease

(diabetic neuropathy; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

(diabetic retinopathy; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related condi-

IT Metabolic disorders

(metabolic syndrome X; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

IT Antidiabetic agents Antihypertensives

Antiobesity agents Atherosclerosis

Diabetes mellitus

Hyperglycemia

Hypertriglyceridemia

Hypolipemic agents

Wound healing

(preparation of human glucagon-like-peptide-1 mimics for use in treatment of

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        516520-74-4P
        516520-75-5P
        516520-77-7P
        516520-79-9P
        516520-81-3P

        516520-82-4P
        516520-84-6P
        516520-86-8P
        516520-87-9P
        516520-89-1P

        516520-91-5P
        516520-93-7P
        516520-95-9P
        516520-97-1P
        516520-99-3P

        516521-01-0P
        516521-03-2P
        516521-05-4P
        516521-07-6P
        516521-08-7P

        516521-10-4P
        516521-10-1P
        516521-12-3P
        516521-13-4P
        516521-14-5P

        516521-23-6P
        516521-18-PP
        516521-12-3P
        516521-12-4P
        516521-22-4P
        516521-23-6P
        516521-22-4P

        516521-28-1P
        516521-24-7P
        516521-30-5P
        516521-31-6P
        516521-32-7P

        516521-33-8P
        516521-34-9P
        516521-35-4P
        516521-31-6P
        516521-32-2P

        516521-34-0P
        516521-34-PP
        516521-43-PP
        516521-32-2P
        516521-32-2P

        516521-34-OP
        516521-34-PP
        516521-32-3P
        516521-32-3P
        516521-32-3P

        516521-34-OP
        516521-34-PP
        516521-32-3P
        516521-32-3P
        516521-32-3P

                RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)
17 150-46-9, Triethyl borate 1973-22-4, 1 Bromo 2 ethylbenzene 4326-36-7 16419-60-6, o Tolylboronic acid 93267-04-0 516521-49-6
                RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)
               90002-36-IP, 2 Ethylphenylboronic acid 112766-18-4P 516521-46-3P 516521-47-4P 516521-48-5P 516521-50-9P 516521-51-0P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
                  (Reactant or reagent)
(Reactant or reagent)
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

IT 51-64-9, Dexamphetamine 94-20-2, Chloropropamide 122-09-8, Phentermine 637-07-0, Clofibrate 657-24-9, Metformin 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 21187-98-4, Gliclazide 22232-71-9, Mazindol 25812-30-0, Gemfibrozii 29094-61-9, Glipizide 49562-28-9, Fenofibrate 65100-240, Academa 27432-03-2, Melihol 753007-55-1 postațiin
```

25812-30-0, Gemfibrozil 29094-61-9, Glipizide 49562-28-9, Penofibrate 56180-94-0, Acarbose 72432-03-2, Miglitol 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 141750-63-2, Nisvastatin 141758-74-9, AC 2993 144288-97-1, TS-962 145599-86-6, Cerivastatin 152755-31-2, LV295427 159183-92-3, L750355 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 170861-63-9, JTT-501 176435-10-2, LV315902 178759-95-0, MD 700 196808-45-4 199113-98-9 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 258345-41-4, GW-409544 262332-17-0, CP 529414 282526-98-1, ATL-962 287714-41-4 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0,

```
(Uses)
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

IT 89750-14-1DP, Glucagon-like peptide 1, mimics 516514-32-2P
516514-38-8P 516514-43-5P 5165114-47-9P 516514-52-6P 516514-52-6P 516514-58-2P 516514-43-5P 516514-47-9P 516514-52-6P 516514-72-0P 516514-58-2P 516514-43-5P 516514-43-P 516514-68-4P 516514-72-0P 516514-73-3P 516514-73-3P 516514-81-PP 516514-81-PP 516514-68-4P 516514-78-0P 516515-09-3P 516515-09-3P 516515-34-PP 516515-48-PP 516515-09-3P 516515-34-PP 516515-34-PP 516515-34-PP 516515-34-PP 516515-50-7P 516515-34-PP 516515-34-PP 516515-34-PP 516515-50-7P 516516-60-2P 516516-60-2P 516516-60-2P 516516-60-2P 516516-60-2P 516516-60-2P 516516-60-2P 516516-60-2P 516516-60-3P 516518-60-3P 516518-
             KAD1129 335149-17-2, ARHO39242 335149-23-0, NVPDPP-728A 335149-25-
             CP331648 430433-17-3, Glipyride 444069-80-1, Axokine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of
                   diabetes and related conditions)
     L33 ANSWER 5 OF 9 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
     STN
    ACCESSION NUMBER: 2003:390202 BIOSIS <<LOGINID::20070124>>
DOCUMENT NUMBER: PREV200300390202
                                                    The glucagon-like peptides: A double-edged therapeutic
                                         sword?.
   AUTHOR(S): Perry, TracyAnn [Reprint Author]; Greig, Nigel H.
CORPORATE SOURCE: Section of Drug Design and Development, Laboratory of
Neurosciences, Gerontology Research Center, National
Institute on Aging, National Institutes of Health, 5600
                                         Nathan Shock Drive, Baltimore, MD, 21224, USA perryt@grc.nia.nih.gov
                                         Trends in Pharmacological Sciences, (July 2003)
Vol. 24, No. 7, pp. 377-383. print.
ISSN: 0165-6147 (ISSN print).
    DOCUMENT TYPE: Article
General Review; (Literature Review)
     LANGUAGE: English
ENTRY DATE: Entered STN: 27 Aug 2003
     Last Updated on STN: 27 Aug 2003
AN 2003:390202 BIOSIS <<LOGINID::20070124>>
     DN PREV200300390202
               The glucagon-like peptides: A double-edged therapeutic sword?.
   AU Perry, TracyAnn [Reprint Author]; Greig, Nigel H.
CS Section of Drug Design and Development, Laboratory of Neurosciences,
Gerontology Research Center, National Institute on Aging, National
Institutes of Health, 5600 Nathan Shock Drive, Baltimore, MD, 21224, USA
             perryt@grc.nia.nih.gov
    SO Trends in Pharmacological Sciences, (July 2003) Vol. 24, No. 7, pp. 377-383. print.
ISSN: 0165-6147 (ISSN print).
             General Review; (Literature Review)
     LA English
ED Entered STN: 27 Aug 2003
   Last Updated on STN: 27 Aug 2003

AB Glucagon-like peptide-1(7-36)-amide (GLP-1) is an endogenous peptide that is secreted from the gut in response to the presence of food. Recent studies have established that GLP-
```

diabetes and related conditions)

diabetes and related conditions)

RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation of human glucagon-like-peptide-1 mimics for use in treatment of

Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

IT Hyperlipidemia

t and its longer-acting analog exendin-4 have multiple synergistic effects on glucose-dependent, insulin secretion pathways of the pancreatic beta-cell and on plasticity in neuronal cells. Recent interest has focused on the development of these peptides as a novel therapeutic strategy for non-insulin-dependent (type 2) diabetes mellitus and associated neuropathy. This is with a view to developing lead compounds, based on neurotrophic action, for central and peripheral degenerative disorders such as stroke and Alzheimer's disease in addition to the peripheral neuropathy associated with type 2 diabetes mellitus. Here, we address recent advances in the biological action of GLP

Here, we address recent advances in the biological action of GLP

-1 and its related analogs.

CC Cytology - Animal 02506

Biochemistry studies - Proteins, peptides and amino acids 10064

Biochemistry studies - Carbohydrates 10068

Pathology - Therapy 12512

Metabolism - Metabolic disorders 13020

Cardiovascular system - Blood vessel pathology 14508 Endocrine - General 17002

Endocrine - General 1/002
Endocrine - Pancreas 17008
Endocrine - Neuroendocrinology 17020
Nervous system - Physiology and biochemistry 20504
Nervous system - Pathology 20506
Pharmacology - General 22002

IT Major Concepts
Endocrine System (Chemical Coordination and Homeostasis); Nervous

System (Neural Coordination); Pharmacology IT Parts, Structures, & Systems of Organisms

beta cells: endocrine system; neuronal cells: nervous system

Alzheimer's disease: behavioral and mental disorders, nervous system

Alzheimer Disease (MeSH)

diabetic neuropathy; endocrine disease/pancreas, metabolic disease, nervous system disease

Diabetic Nephropathies (MeSH)

IT Diseases

stroke: nervous system disease, vascular disease

Cerebrovascular Disorders (MeSH)

Diseases
 type 2 diabetes mellitus: endocrine disease/pancreas, metabolic disease
 Diabetes Mellitus, Non-Insulin-Dependent (MeSH)
 Chemicals & Biochemicals

glucagon-like peptide-1(7-36)-amide; glucose; insulin IT Miscellaneous Descriptors

drug development

the patients, known duration of diabetes, metabolic control, BMI, or residual beta-cell pancreatic function. Endogenous creatinine clearance was significantly reduced under conditions of overt diabetic nephropathy, compared with normo and microalbuminuric patients (p<0.01). Urinary excretion of GLP-1 was significantly higher in normoalbuminuric patients compared to controls (490.4+211.5 vs. 275.5+132.1 pg/min; p<0.05), with further increase under incipient diabetic nephropathy conditions (648.6+305 pg/min; p<0.01). No significant difference resulted, in contrast, between residual beta-cell pancreatic function. Endogenous creatinine clearance macroproteinuric patients and non-diabetic subjects. Taking all patients macroproteinuric patients and non-diabetic subjects. Taking all patients examined into account, a significant positive relationship emerged between urinary GLP-1 and creatinine clearance (p=0.004). In conclusion, an early tubular impairment in type 2 diabetes would occur before the onset of glomerular permeability alterations. The tubular dysfunction seems to evolve with the development of persistent microalbuminuria. Finally, the advanced tubular involvement, in terms of urinary GLP1 excretion, under overt diabetic nephropathy conditions would be masked by severe concomitant glomerular damage with the occusitence of both alterations resulting in a peptide excretion similar to country subjects. similar to control subjects.

Schemistry studies - Proteins, peptides and amino acids 10064
Metabolism - Metabolic disorders 13020
Urinary system - Pathology 15506
Endocrine - General 17002

Endocrine - Pancreas 17008

Clinical Endocrinology (Human Medicine, Medical Sciences); Nephrology (Human Medicine, Medical Sciences)

diabetic nephropathy: endocrine disease/pancreas, metabolic disease, urologic disease Diabetic Nephropathies (MeSH)

type 2 diabetes mellitus: endocrine disease/pancreas, metabolic disease, non-insulin-dependent diabetes mellitus Diabetes Mellitus, Non-Insulin-Dependent (MeSH)

17 Chemicals & Biochemicals creatinine; glucagon-like peptide 1: renal tubular integrity indicator; glucagon-like peptide 1 7-36 amide [GLP-1 7-36 amide]: urinary excretion

IT Miscellaneous Descriptor glomerular permeability ORGN Classifier

Hominidae 86215 Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

```
RN 118549-37-4 (glucagon-like peptide-1(7-36)-amide)
        50-99-7Q (glucose)
58367-01-4Q (glucose)
        9004-10-8 (insulin)
 L33 ANSWER 6 OF 9 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
       DUPLICATE I
ACCESSION NUMBER: 2001:506591 BIOSIS <<LOGINID::20070124>> DOCUMENT NUMBER: PREV200100506591
                               Urinary excretion of glucagon-like peptide 1 (GLP
-1) 7-36 amide in human type 2
                              (non-insulin-dependent) diabetes mellitus.

S): Lugari, R. [Reprint author]; Ugolotti, D.; Dei Cas, A.;
AUTHOR(S): Lugan, K. [Repnnt author]; Ugolotti, D.; Del Cas, A.;
Barilli, A. L.; lotti, M.; Marani, B.; Orlandini, A.;
Gnudi, A.; Zandomeneghi, R.
CORPORATE SOURCE: Cattedra di Endocrinologia, Via Gramsci 14, 43100, Parma,
Italy endoparm@iprumiv.cce.unipr.it

SOURCE: Hormone and Metabolic Research, (September, 2001)

Vol. 33, No. 9, pp. 568-571, print.

CODEN: HMMRA2. ISSN: 0018-5043.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 31 Oct 2001

Last Updated on STN: 23 Feb 2002

AN 2001:506591 BIOSIS <<LOGINID::20070124>>

DN PREV200100506591

I. Utimary expertion of glues goog-like pertide 1 (GI Pa)
DN PREV200100506591

Il Urinary excretion of glucagon-like peptide 1 (GLP-1)
7-36 amide in human type 2 (non-insulin-dependent) diabetes mellitus.

AU Lugari, R. (Reprint author); Ugolotti, D.; Dei Cas, A.; Barilli, A. L.;

lotti, M.; Marani, B.; Orlandini, A.; Gnudi, A.; Zandomeneghi, R.

CS Cattedra di Endocrinologia, Via Gramsci 14, 43100, Parma, Italy
endoparm@ipruniv.cce.unipr.it

SO Hormone and Metabolic Research, (September, 2001) Vol. 33, No.
9, pp. 568-571. print.

CODEN: HMMRA2. ISSN: 0018-5043.

DT Article
 DT Article
LA English
 ED Entered STN: 31 Oct 2001
Last Updated on STN: 23 Feb 2002
 AB The urinary excretion of insulinotropic glucagon-like peptide 1 (
GLP-1) was investigated as an indicator of renal tubular
       integrity in 10 healthy subjects and in 3 groups of type 2 diabetic patients with different degrees of urinary albumin excretion rate. No
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significant difference emerged between the groups with respect to age of

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Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 60-27-5 (creatinine)
  L33 ANSWER 7 OF 9 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights
  reserved on STN
ACCESSION NUMBER: 96034762 EMBASE <<LOGINID::20070124>>
 ACCESSION NUMBER: 96034/62 EMBASE < LOCINID::200/0124
DOCUMENT NUMBER: 1996034762
TITLE: Gastric emptying, glucose responses, and insulin secretion after a liquid test meal: Effects of exogenous glucagon-like peptide-1 (GLP-1)-(7-36) amide in type 2 (noninsulin-dependent) diabetic patients.

AUTHOR: Willins B.; Werner J.; Holst J.J.; Orskov C.; Creutzfeldt
                           W : Nauck M.A.
 CORPORATE SOURCE: Department of Medicine, Ruhr-University Bochum, Knappschafts-Krankenhaus, In der Schornau 23-25,44892 Bochum, Germany

SOURCE: Journal of Clinical Endocrinology and Metabolism, (
                           1996) Vol. 81, No. 1, pp. 327-332. .
ISSN: 0021-972X CODEN: JCEMAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
037 Drug Literature Index
English
SIMMANY
LANGUAGE: English
SUMMARY LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 1996
Last Updated on STN: 20 Feb 1996
AN 96034762 EMBASE <<LOGINID::20070124>>
  DN 1996034762
 TI Gastric emptying, glucose responses, and insulin secretion after a liquid test meal: Effects of exogenous glucagon-like peptide-1 (GLP-1)-(7-36) amide in type 2 (noninsulin-dependent) diabetic
```

17(7-30) and the intype 2 (nonmounted percent) discenting the patients.

AU Willms B.; Werner J.; Holst J.J.; Orskov C.; Creutzfeldt W.; Nauck M.A.

CS Department of Medicine, Ruhr-University Bochum, Knappschafts-Krankenhaus, In der Schormau 23-25,44892 Bochum, Germany

SO Journal of Clinical Endocrinology and Metabolism, (1996) Vol.

81, No. 1, pp. 327-332. . ISSN: 0021-972X CODEN: JCEMAZ

037 Drug Literature Index

CY United States DT Journal; Article FS 003 Endocrinology

Organism Name

human: patient

```
SL English
    ED Entered STN: 20 Feb 1996
Last Updated on STN: 20 Feb 1996

AB The aim of the study was to investigate whether inhibition of gastric emptying of meals plays a role in the mechanism of the blood glucose-lowering action of glucagon-like peptide-1-(7-3-6) amide [ GLP-1-(7-3-6) amide] in type 2 diabeties. Eight poorly controlled type 2 diabetic patients (age, 58 ± 6 yr, body mass index, 30.0 ± 5.2 kg/m²; hemoglobin A(1c), 10.5 ± 1.2%) were studied in the fasting state (plasma glucose, 11.1 ± 1.1 mmol/L). A liquid meal of 400 mL containing 8% amino acids and 50 g sucrose (327 Kcal) was administered at time zero by a nasogastric tube. Gastric volume was determined by a dye dilution technique using phenol red. In randomized order, GLP-1-(7-3-6) amide (1.2 pmol/kg· min; Saxon Biochemicals) or placebo (0.9% NaCl with 1% human serum albumin) was infused between -30 and 240 min. In the control experiment, gastric emptying was completed within 120 min, and plasma glucose, insulin, C-peptide, GLP-1-(7-3-6) amide, and glucagon concentrations transiently increased. With exogenous GLP-1-(7-3-6) amide (plasma level, apprx. 70 pmol/L), gastric volume
                 Last Updated on STN: 20 Feb 1996
             concentrations transiently increased. With exogenous GLP-1-(7-36) amide (plasma level, apprx.70 pmoVL), gastric volume remained constant over the period it was measured (120 min; P < 0.0001 vs. placebo), and plasma glucose fell to normal fasting values (5.4 \pm 0.7 mmoVL) within 3-4 h, whereas insulin was stimulated in most, but not all, patients, and glucagon remained at the basal level or was slightly suppressed. In conclusion, GLP-1-(7-36) amide inhibits gastric emptying in type 2 diabetic patients. Together with the stimulation of insulin and the inhibition of glucagon secretion, this effect probably contributes to the blood glucose-lowering action of GLP-1-(7-36) amide in two 2-diabetic patients when
               GLP-1-(7-36) amide in type 2-diabetic patients when studied after meal ingestion. At the degree observed, inhibition of
                gastric emptying, however, must be overcome by tachyphylaxis, reduction in dose, or pharmacological interventions so as not to interfere with the therapeutic use of GLP-1-(7-36) amide in type 2
  diabetic patients.

CT Medical Descriptors:
                 *insulin release
*non insulin dependent diabetes mellitus: DT, drug therapy
                   non insulin dependent diabetes mellitus: TH, therapy
                    stomach emptying
               tluba'
                aged
                 article
                 clinical article
                clinical trial
```

LA English

controlled study

```
heterotopic pancreas and kidney transplantation.

AUTHOR(S): Nauck, M. A. [Reprint author]; Buesing, M.; Orskov, C.; Siegel, E. G.; Talartschik, J.; Baartz, A.; Baartz, T.; Hopt, U. T.; Becker, H.-D.; Creutzfeldt, W.

CORPORATE SOURCE: Div. Gastroenterol. and Endocrinol., Dep. Med., Georg August Univ., Robert-Koch-Strasse 40, W-3400 Goettingen, Germany

SOURCE: Acta Diabetologica, (1993) Vol. 30, No. 1, pp. 39-45.

CODEN: ACDAEZ. ISSN: 0940-5429.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 8 Sep 1993

Last Updated on STN: 3 Jan 1995

AN 1993-408694 BIOSIS <<LOGINID::20070124>>

DN PREV199396074419

TI Preserved incretin effect in type 1 diabetic patients with end-stage nephropathy treated by combined heterotopic pancreas and kidney transplantation.

AU Nauck, M. A. [Reprint author]; Buesing, M.; Orskov, C.; Siegel, E. G.; Talartschik, J.; Baartz, A.; Baartz, T.; Hopt, U. T.; Becker, H.-D.; Creutzfeldt, W.

CS Div. Gastroenterol. and Endocrinol., Dep. Med., Georg August Univ., Robert-Koch-Strasse 40, W-3400 Goettingen, Germany

SO Acta Diabetologica, (1993) Vol. 30, No. 1, pp. 39-45.

CODEN: ACDAEZ. ISSN: 0940-5429.

DT Article

LA English

ED Entered STN: 8 Sep 1993

Last Updated on STN: 3 Jan 1995

AB Insulin secretion is stimulated better by oral than by intravenous glucose (incretin effect). The contribution of the autonomic nervous system to the incretin effect after oral glucose in humans is unclear. We therefore examined nine type 1 diabetic (insulin-dependent) patients with end-stage nephropathy, studied after combined heterotopic pancreas and kidney transplantation, and 7 non-diabetic kidney recipients (matched for creatinine clearance and immunosuppressive medication). The release of gastric inhibitory polypeptide (GIP) and glucagon-like peptide 1 (GIP-1) immunoreactivity and B cell secerctory responses (IR insulin and C-peptide) to oral (50 g) and "isoglycaemic" intravenous glucose (identical glycaemic profile) were measured by radioimmunosasay. The difference in B cell respon
```

contribution of the enteroinsular axis to the response after oral glucose (incretin effect). Insulin responses after the oral glucose challenge

were similar in the two patient groups despite systemic venous drainage of the pancreas graft in the pancreas-kidney-transplanted group. In both

```
diabetic angiopathy: CO, complication
      diabetic nephropathy: CO, complication
diabetic neuropathy: CO, complication
diabetic retinopathy
      drug effect
      drug mechanism
female
      glucagon release
      glucose blood level
      hormone inhibition
      human
      hypertension: DT, drug therapy
      intravenous drug administration
     postprandial state
     priority journal randomized controlled trial
     Drug Descriptors:
•glucagon like peptide 1 [7-36] amide: CM, drug comparison
      *Slucagon like peptide 1 [7-30] amice: CM, arug compare slucagon like peptide 1 [7-36] amide: DT, drug therapy slucagon like peptide 1 [7-36] amide: PD, pharmacology slucagon like peptide 1 [7-36] amide: CT, clinical trial slucase: EC, endogenous compound insulin: EC, endogenous compound
     acarbose: DT, drug therapy
captopril plus hydrochlorothiazide: DT, drug therapy
     captopri pius nydrochiorotniazide: D
glibenclamide: DT, drug therapy
isosorbide dinitrate: DT, drug therapy
metformin: DT, drug therapy
metoprolol: DT, drug therapy
metoprotoi: DT, drug therapy
nifedipine: DT, drug therapy
placebo: CM, drug comparison
RN (glucagon like peptide 1 [7-36] amide) 119637-73-9; (glucose) 50-99-7,
84778-64-3; (insulin) 9004-10-8; (acarbose) 56180-94-0; (glibenclamide)
10238-21-8; (isosorbide dinitrate) 87-33-2; (metformin) 1115-70-4,
657-24-9; (metoprolol) 37350-58-6; (nifedipine) 21829-25-4
CO Saxon (Germany)
L33 ANSWER 8 OF 9 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
     DUPLICATE 2
ACCESSION NUMBER: 1993:408694 BIOSIS <<LOGINID::20070124>>
DOCUMENT NUMBER: PREV199396074419
TITLE: Preserved incretin effect in type 1 diabetic patients with
                       end-stage nephropathy treated by combined
```

groups GIP and GLP-1 increased after oral but not after intravenous glucose, and B cell secretory responses were significantly smaller (by 55.2 + -7.7% and 46.5 + -12.5%, respectively) with 'isoglycaemic" intravenous glucose infusions. The lack of reduction in the incretin effect in pancreas-kidney-transplanted patients, whose functioning pancreas is denervated, indicates a lesser role for the nervous system and a more important contribution of circulating incretin hormones in mediating the enteroinsular axis in man.

CC Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Anatomy and Histology - Surgery 11105
Anatomy and Histology - Regeneration and transplantation 11107
Pathology - Therapy 12512
Metabolism - Carbohydrates 13004
Metabolism - Carbohydrates 13004
Metabolism - Proteins, peptides and amino acids 13012
Metabolism - Peroteins, peptides and amino acids 13012
Metabolism - Metabolic disorders 13020
Digestive system - General and methods 14001
Digestive system - Pathology 14006
Urinary system - Pathology 15506
Endocrine - Pancreas 17008

IT Major Concepts
Endocrine System (Chemical Coordination and Homeostasis);
Gastroenterology (Human Medicine, Medical Sciences); Metabolism;
Physiology; Surgery (Medical Sciences); Urology (Human Medicine, Medical Sciences)
IT Chemicals & Biochemicals
PNCRETIN; GLUCAGON; INSULIN

Miscellaneous Descriptors
ANTIDIABETIC-DRUG; DIABETIC NEUROPATHY; ENZYME INHIBITOR-DRUG
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Hominidae
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 54241-84-8 (INCRETIN)
9007-92-5 (GLUCAGON)
9004-10-8 (INSULIN)

L33 ANSWER 9 OF 9 MEDLINE on STN
ACCESSION NUMBER: 92288534 MEDLINE <LOGINID::20070124>>
DOCUMENT NUMBER: PubMed ID: 1600330

```
TITLE:
                                 Basal and nutrient-stimulated pancreatic and
                          gastrointestinal hormone concentrations in type-1-diabetic
patients after successful combined pancreas and kidney
 AUTHOR: Nauck M A; Busing M; Orskov C; Siegel E G; Talartschik J;
Baartz A; Baartz T; Holzer H; Hopt U T; Ebert R; +
CORPORATE SOURCE: Abteilung Gastroenterologie und Endokrinologie,
                         Georg-August-Universitat, Gottingen.
The Clinical investigator, (1992 Jan) Vol. 70,
GERMANY: Germany, Federal Republic of Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: ENTRY MONTH: 199207
ENTRY DATE: 199207
 No. 1, pp. 40-8.

Journal code: 9207154. ISSN: 0941-0198.

PUB. COUNTRY: GERMANY: Germany, Federal Republic of DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
 ENIRY DATE: Entered $110.29 Jul 1992
Last Updated on $TN: 24 Jul 1992
Entered Medline: 13 Jul 1992
AN 92288534 MEDLINE <<LOGINID::20070124>>
DN PubMed ID: 1600330
  TI Basal and nutrient-stimulated pancreatic and gastrointestinal hormone
concentrations in type-1-diabetic patients after successful combined
 contentiation in type I varieties and side secessive contention pancreas and kidney transplantation.

AU Nauck M A; Busing M; Orskov C; Siegel E G; Talartschik J; Baartz A; Baartz T; Holzer H; Hopt U T; Ebert R; + CS _Abteilung Gastroenterologie und Endokrinologie, Georg-August-Universitat,
 Gottingen.
SO The Clinical investigator, (1992 Jan) Vol. 70, No. 1, pp. 40-8.
Journal code: 9207154. ISSN: 0941-0198.
 CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
  LA English
  FS Priority Journals
 EM 199207
ED Entered STN: 24 Jul 1992
       Last Updated on STN: 24 Jul 1992
Entered Medline: 13 Jul 1992
  AB The secretion of pancreatic and gastrointestinal hormones in the basal
       state and after not paneteate and gastomizestina informizes in the obsain
state and after notifient stimuli (50 g glucose, 50 g protein, or 30 g
triglyceride administered on separate occasions) was assessed in ten
previously type-1-diabetic patients after successful combined kidney and
panereas transplantation (systemic venous drainage). Pasting values were
       compared to matched non-diabetic kidney-transplanted patients and related to kidney function (endogenous creatinine clearance) and to the type and
        dosage of immunosuppressive medication. In the fasting state, only IR
 PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S.
Ser. No. 273,975.
                                CODEN: USXXCO
  DOCUMENT TYPE:
                                                       Patent
 LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
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PATENT NO.
                                                        KIND DATE
                                                                                                      APPLICATION NO.
                                                                                                                                                                     DATE
       US 2004127423
                                                        A1 20040701
A1 20031016
                                                                                                    US 2003-419399
                                                                                                                                                           20030421
           IS 2003195157 A1 20031016 US 2002-273975 20021018 <--
VO 2004094461 A2 20041014 WO 2004-US12374 20040421
VO 2004094461 A3 20050915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, LS, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TI, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD. TG
                                                                                                   US 2002-273975
        WO 2004094461
                                                    A2 20060118 EP 2004-760098
                                                                                                                                                   20040421
             R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR US 2001-342015P P 20011018
PRIORITY APPLN. INFO.:
PRIORITY APPLN. INFO:: US 2002-273975 A2 20021018
US 2003-419399 A 20030421
WO 2004-US12374 W 20040421
AN 2004:533962 CAPPLUS <<LOGINID::20070124>>
DN 141:82335
ED Entered STN: 02 Jul 2004
TI Human glucagon-like-peptide-1 mimics and their antidiabetic effects
IN Natarajan, Sesha Iyer, Mapelli, Claudio; Bastos, Margarita M.;
Bernatowicz, Michael; Lee, Ving; Ewing, William R.
SO U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 273,975.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K038-10
ICS C07K007-08
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PATENT INFORMATION:

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insulin concentrations were higher in pancreas-kidney-transplanted patients (by 88%; P=0.001) than in the kidney graft recipients. There were significant inverse correlations of plasma C-peptide, GIP, and gastrin immunoreactivity to endogenous creatinine clearance (kidney function). In response to nutrients, insulin secretion (IR insulin, C-peptide) was significantly stimulated by glucose, and - to a lesser degree - also by protein. Pancreatic glucagon was suppressed by glucose and stimulated by protein ingestion. GIP was raised after glucose and triglyceride more than after protein (P=0.0003). GLP- 1 immunoreactivity was stimulated by all nutrients, with a tendency towards higher responses to protein and fat (P=0.06). Gastrin was mainly raised by protein. In conclusion, the overall pattern of pancreatic and gastrointestinal hormone release is normal in patients after combined pancreas-kidney-transplantation, but there are some peculiarities due to (a) systemic venous drainage of the pancreas graft
       peculiarities due to (a) systemic venous drainage of the pancreas graft (elevated fasting IR insulin) and (b) impaired kidney function (negative
       correlation of fasting plasma values to endogenous creatinine clearance for C-peptide, GIP, and gastrin).(ABSTRACT TRUNCATED AT 250 WORDS)
CT Check Tags: Female; Male
        Adult
Blood Glucose: ME, metabolism
       Diabetes Mellitus, Type 1: BL, blood

*Diabetes Mellitus, Type 1: SU, surgery
Diabetic Nephropathies: BL, blood

*Diabetic Nephropathies: SU, surgery
        *Gastrointestinal Hormones: BL, blood
        Kidney Function Tests
        *Kidney Transplantation: PH, physiology
        Middle Aged
        *Pancreas Transplantation: PH, physiology
Pancreatic Function Tests
*Pancreatic Hormones: BL, blood
Research Support, Non-U.S. Gov't
CN 0 (Blood Glucose); 0 (Gastrointestinal Hormones); 0 (Pancreatic Hormones)
D Ibib all L34 1-9
L34 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
                                                                     2004:533962 CAPLUS <<LOGINID::20070124>>
141:82335
ACCESSION NUMBER:
DOCUMENT NUMBER:
                                     Human glucagon-like-peptide-1 mimics and their antidiabetic effects
INVENTOR(S): Natarajan, Sesha Iyer, Mapelli, Claudio; Bastos,
Margarita M.; Bernatowicz, Michael; Lee, Ving; Ewing,
                                     William R.
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INCL 514015000; 530328000
CC 1-10 (Pharmacology)
    Section cross-reference(s): 2, 34, 63
FAN.CNT 2
    PATENT NO.
                               KIND DATE
                                                          APPLICATION NO.
PI US 2004127423
       A1 20040701 US 2003-419399
                                                                                       20030421
    US 2003 195 157
     WO 2004094461
     WO 2004094461
1U, 1U
EP 1615633 A2 20060118 EP 2004-760098 20040421
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
PRAI US 2001-342015P P 20011018
           TD. TG
    US 2002-273975 A2 20021018
US 2003-419399 A 20030421
WO 2004-US12374 W 20040421
 PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES
 US 2004127423 ICM A61K038-10
              ICS C07K007-08
INCL 514015000; 530328000
              IPCI A61K0038-10 [ICM,7]; C07K0007-08 [ICS,7]; C07K0007-00 [ICS,7,C*]
[ICS,7,C*]

IPCR A61K0038-00 [N,C*]; A61K0038-00 [N,A]; C07K0014-435

[1,C*]; C07K0014-605 [1,A]

NCL 514/015.000; 530/328.000

ECLA C07K014/605

US 2003195157 IPC1 A61K0038-10 [ICM,7]; A61K0038-08 [ICS,7]; C07K0007-08

[ICS,7]; C07K0007-06 [ICS,7]; C07K0007-00 [ICS,7,C*]

IPCR A61K0038-00 [N,C*]; A61K0038-00 [N,A]; C07K0014-435
              [LC*]; C07K0014-605 [LA]

NCL 514/016.000; 514/017.000; 530/328.000; 530/329.000

ECLA C07K014/605
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WO 2004094461 IPCI C07K [ICM,7]
IPCR A61K0038-00 [LC*]; A61K0038-00 [LA]; A61K0038-02
[LC*]; A61K0038-02 [LA]; A61K0038-08 [LC*];
A61K0038-08 [LA]; A61K0038-10 [LC*]; A61K0038-10
[LA]; C07K [LS]; C07K0007-00 [LC*]; C07K0007-02
[IA]; C07K0007-04 [LA]; C07K0007-08 [LA]
IPCI A61K0038-00 [ICS,7]; C07K0007-02 [ICS,7]; A61K0038-10
[ICS,7]; A61K0038-08 [ICS,7]; C07K0007-02 [ICS,7]; C07K0007-04 [ICS,7]; C07K0007-06 [ICS,7]; C07K0007-06 [ICS,7]; C07K0007-06
                                                                                                                                                                                                                                                                                                                                                                                                                                                 RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cholesterol ester-exchanging; human glucagon-like-peptide-1 mi
                                    [ICS,7,C*]
IPCR A61K0038-00 [LC*]; A61K0038-00 [LA]; A61K0038-02
                                                [LA]; C07K0038-02 [LA]; A61K0038-08 [LC*]; A61K0038-08 [LA]; A61K0038-08 [LA]; A61K0038-08 [LA]; A61K0038-10 [LC*]; A61K0038-10 [LC*]; A61K0038-10 [LA]; C07K007-02 [LA]; C07K007-04 [LA]; C07K007-08 [LA]
AB The invention discloses human glucagon-like peptide-1 (GLP-1) peptide minies that mimic the biol. activity of the native
         GLP-1 peptide and thus are useful for the treatment or prevention of diseases or disorders associated with GLP activity. Further,
            the invention provides novel, chemical modified peptides that not only
          stimulate insulin secretion in type II diabetics, but also produce other beneficial insulinotropic responses. These synthetic peptide GLP
          -1 mimics exhibit increased stability to proteolytic cleavage
making them ideal therapeutic candidates for oral or parenteral
             administration.
 ST human glucagon peptide mimic prepn diabetes antidiabetic insulin
            RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
          (Biological study); USES (Uses)

(ALBP (adipocyte lipid-binding protein); human glucagon-like-peptide-l mimics and their antidiabetic effects)
  IT Lipoprotein receptors
            RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LDL; human glucagon-like-peptide-1 mimics and their antidiabetic
                  effects)
          RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
         (Rispanding) (Risp
                 (antiatherosclerotics; human glucagon-like-peptide-1 mimics and their
                  antidiabetic effects)
IT Drug delivery systems
(capsules; human glucagon-like-peptide-1 mimics and their antidiabetic
```

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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (human glucagon-like-peptide-1 mimics and their antidiabetic effects)
(human glucagon-like-peptide-1 mimics and their antidiabeti
IT Drug delivery systems
(injections; human glucagon-like-peptide-1 mimics and their
         antidiabetic effects)
       Metabolic disorders
         (metabolic syndrome X; human glucagon-like-peptide-1 mimics and their
          antidiabetic effects)
       Drug delivery systems
         (microparticles; human glucagon-like-peptide-1 mimics and their
           intidiabetic effects)
 IT Diabetes mellitus
         (non-insulin-dependent; human glucagon-like-peptide-1 mimics and their
         antidiabetic effects)
       Antidiabetic agents
      Drug delivery systems
         (oral; human glucagon-like-peptide-1 mimics and their antidiabetic
 IT Drug delivery systems
         (suspensions; human glucagon-like-peptide-1 mimics and their antidiabetic effects)
       Drug delivery systems
(tablets; human glucagon-like-peptide-1 mimics and their antidiabetic
         effects)
 IT Peroxisome proliferator-activated receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
(a; human glucagon-like-peptide-1 mimics and their antidiabetic
 IT Peroxisome proliferator-activated receptor
     RL: BSU (Biological study, unclassified); BIOL (Biological study) (g; human glucagon-like-peptide-1 mimics and their antidiabetic
IT 51-61-6, Dopamine, biological studies 56-81-5, Glycerol, biological studies 9001-62-1, Lipase 9028-35-7, 3-Hydroxy-3-methylglutaryl CoA reductase 9029-60-1, Lipoxygenase 9033-06-1, Glucosidase 9077-14-9, Squalene synthetase 63551-74-6, Lipoxygenase 90002-36-1, 2-Ethylphenyl
       RL: BSU (Biological study, unclassified); BIOL (Biological study)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(human glucagon-like-peptide-1 mimics and their antidiabetic effects)

IT 516514-32-2P 516514-38-8P 516514-43-5P 516514-47-9P 516514-52-6P
516514-52-9P 516514-58-2P 516514-43-7P 516514-64-0P 516514-68-4P
516514-72-0P 516514-75-3P 516514-78-6P 516514-81-1P 516514-84-4P
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516515-06-3P 516515-09-6P 516515-14-3P 516515-18-7P 516515-22-3P
516515-22-3P 516515-22-3P 516515-32-7P
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their antidiabetic effects)
     Kidney, disease
     (diabetic nephropathy; human glucagon-like-peptide-1 mimics
       and their antidiabetic effects)
    Nerve, disease
      (diabetic neuropathy; human glucagon-like-peptide-1 mimics and their
      antidiabetic effects)
     Eve. disease
      (diabetic retinopathy; human glucagon-like-peptide-1 mimics and their
       antidiabetic effects)
     Transport proteins
   RL: BSU (Biological study, unclassified); BIOL (Biological study)
     (dopamine transporter, human glucagon-like-peptide-1 mimics and their antidiabetic effects)
IT 5-HT reuptake inhibitors
   Antihypertensives
    Antiobesity agents
   Appetite depressants
   Atherosclerosis
     Diabetes mellitus
   Human
   Hyperglycemia
     Hypertension
   Hypertriglyceridemia
   Hypolipemic agents
    Signal transduction, biological
   Wound healing
b3-Adrenoceptor agonists
    (human glucagon-like-peptide-1 mimics and their antidiabetic effects)
Fatty acids, biological studies
   Glucagon-like peptide-1 receptors
Hyperlipidemia
   Thyroid hormone receptors
   RL: BSU (Biological study, unclassified); BIOL (Biological study) (human glucagon-like-peptide-1 mimics and their antidiabetic effects)
IT Peptides, biological studies
   repnies, noingical studies
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
      (human glucagon-like-pentide-1 mimics and their antidiabetic effects)
IT Sulfonylureas
```

effects) Proteins

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$16515-46-IP $16515-50-7P $16515-55-2P $16515-59-6P $16515-63-2P $16515-68-7P $16515-72-3P $16515-76-7P $16515-80-3P $16515-84-7P $16515-68-7P $16515-92-7P $16515-96-IP $16516-01-IP $16516-06-6P $16516-10-IP $16516-06-2P $16516-13-7P $16516-33-7P $16516-33-P $16516-60-2P $16516-60-2P $16516-60-2P $16516-60-2P $16516-60-2P $16516-60-2P $16516-60-2P $16516-60-2P $16516-60-2P $16516-76-0P $16516-98-6P $16516-83-IP $16516-83-IP $16516-76-0P $16516-76-0P $16516-98-P $16516-92-P $16516-93-P $16517-09-P $16517-09-P $16517-33-P $16517-33-P $16517-33-P $16517-33-P $16517-33-P $16517-33-P $16517-33-P $16517-30-P $16517-30-P $16517-30-P $16517-30-P $16517-30-P $16517-30-P $16517-30-P $16517-30-P $16518-30-2P $16518-30-2P $16518-30-2P $16518-30-2P $16518-30-2P $16518-40-P $16518-30-P $16518-40-P $16
                                $16519-15-6P $16519-18-9P $16519-21-4P $16519-24-7P $16519-27-0P $16519-32-7P $16519-32-7P $16519-59-8P $16519-59-8P $16519-67-8P $16519-67-8P $16519-59-8P $16519-67-8P $16519-67-8P $16519-97-9P $16519-99-8P $16520-03-9P $16520-09-9P $16520-13-1P $16520-17-5P $16520-22-2P $16520-42-6P $16520-49-9P $16520-33-5P $16520-38-8P $16520-33-1P $16520-43-8P $16520-43-8P $16520-33-1P $16520-43-8P $16520-33-1P $16520-33-9P $1652
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                                              RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic
                                         preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human glucagon-like-peptide-1 mirnies and their antidiabetic effects)
T7 713497-79-1P 713497-81-5P 713497-83-7P 713497-85-9P
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RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Inturnan glucagon-like-peptide-1 mimics and their antidiabetic effects)
(IT 51-64-9, Dexamphet-amine 56-03-1, Biguanide 94-20-2, Chloropropamide 122-09-8, Phentermine 637-07-0, Clofibrate 657-24-9, Mctformin 94-34-5-10, Fibrica cid, derivs. 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 21137-98-4, Gliclazide 22232-71-9, Mazindol 25812-30-0, Genfibrozil 29094-61-9, Glipizide 49562-28-9, Penofibrate 54870-28-9, Meglitinide 56180-94-0, Acarbose 72432-03-2, Miglitol 75300-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 89750-14-1, Glucagon-like peptide 1 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 122320-73-4, Rosigiltazone 134523-00-5, Ator-vastatin 135062-02-1, Repaglinide 141750-63-2, Nisvastatin 141758-74-9, AC2993 144288-97-1, TS-962 145599-86-6, Cerivastatin 152755-31-2, LY295427 159183-92-3, L750355 161600-01-7, Isaglitazone 16518-60-1, Avasimibe 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 196808-45-4 199113-98-9, NN-2344 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 258345-41-4, GW-409544 262352-17-0, CP 529414 282526-98-1, ATI-962 287714-41-4 335149-08-1, L895465 335149-14-9, R-119702 335149-15-0, KAD1129 335149-17-2, AR-H039242 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipyride 444069-80-1, Axokine RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (human glucagon-like-peptide-1 mimics and their antidiabetic effects)

IT 150-46-9, Triethylborate 358-23-6, Triflic anhydride 1973-22-4, 1-Bromo-2-ethylborate 3426-36-7 16419-60-6, O-Tolylboronic acid 32911-69-1 93267-04-0 516521-49-6 713497-86-0
RL: RCT (Reactant); RACT (Reactant or reagent) (human glucagon-like-peptide-1 mimics an
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RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; human glucagon-like-peptide-1 mimics and their antidiabetic effects)

IT 54249-88-6, Dipeptidyl peptidase IV

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inhibitors
IN Daisy, Joe
PA Pfizer Products Inc., USA
SO Eur. Pat. Appl., 71 pp.
CODEN: EPXXDW
    ICS C07D491-04; C07D209-52; A61K031-407; A61P003-10; A61P009-10; C07D495-14; C07D333-00; C07D209-00; C07D307-00
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 2
     PATENT NO.
                                      KIND DATE APPLICATION NO. DATE
         P 1391460 A1 20040225 EP 2003-20676 20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
Pl EP 1391460
             IE, FI, CY
                                     A2 20010404 EP 2000-308131
                                     A3 20010627
     EP 1088824
        F 108824 B1 20040107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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E, SI, LT, LV, FI, RO
US 2002183369 A1 20021205 US 2002-117370
US 6576653 B2 20030610
US 2003195361 A1 20031016 US 2003-367002
US 6828343 B2 20041207
PRAI US 1999-157148P P 19990930
EP 2000-308131 A3 20000918
US 2000-670759 A3 20000927
US 2002-117370 A3 20020405
CLASS
                                                                                                            20020405 <--
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                           CLASS PATENT FAMILY CLASSIFICATION CODES
                 60 ICM C07D495-04
ICS C07D491-04; C07D209-52; A61K031-407; A61P003-10;
A61P009-10; C07D495-14; C07D333-00; C07D209-00;
                         C07D307-00
                        COTD0495-04 [ICM,7]; C07D0491-04 [ICS,7]; C07D0491-00 [ICS,7,C*]; C07D0209-52 [ICS,7]; A61K0031-407 [ICS,7]; A61P0003-10 [ICS,7]; A61P0003-10 [ICS,7]; A61P0009-10 [ICS,7]; A61P0009-10 [ICS,7]; A61P0009-10 [ICS,7,C*]; C07D0495-14 [ICS,7]; C07D0495-00 [ICS,7,C*]; C07D0333-00 [ICS,7]; C07D0209-00 [ICS,7]; C07D0307-00
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ECLA C07D491/04+307B+209B; C07D495/04+333B+209B;

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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (inhibitors; human glucagon-like-peptide-1 mimics and their
antidiabetic effects)

IT 9004-10-8, Insulin, biological studies
    RL: BSU (Biological study, unclassified); BIOL (Biological study) (resistance, hyperinsulinemia; human glucagon-like-peptide-1 mimics and
        their antidiabetic effects)
L34 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:157498 CAPLUS <<LOGINID::20070124>>
DOCUMENT NUMBER: 140:199313
                          Preparation of fused pyrrolylcarboxamides as glycogen
                     phosphorylase inhibitors
processory are indutors

NVENTOR(S: Daisy, Joe
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 71 pp.
CODEN: EFXXDW
DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:
    PATENT NO.
                                KIND DATE
                                                          APPLICATION NO.
       P 1391460 A1 20040225 EP 2003-20676 20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
    EP 1391460
           IE, FI, CY
                               A2 20010404 EP 2000-308131
    EP 1088824
                              A3 20010627
    E: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
US 2002183369 A1 20021205 US 2002-117370 20020405 <--
     US 6576653 B2 20030610
US 2003195361 A1 20031016 US 2003-367002
                                                                                         20030214 <--
US 6828343 B2 20041207 PRIORITY APPLN. INFO.:
                                                          US 1999-157148P
                                     EP 2000-308131 A3 20000918
US 2000-670759 A3 20000927
                                      US 2002-117370 A3 20020405
MARPAT 140:199313
                                     US 2002-117370
OTHER SOURCE(S): MARPAT 140:199313
AN 2004:157498 CAPLUS <<LOGINID::20070124>>
ED Entered STN: 26 Feb 2004
Ti Preparation of fused pyrrolýlcarboxamides as glycogen phosphorylase
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CO7D495/14+333B+333B+209B

EP 1088824

IPCI CO7D0495-04 [ICM,6]; CO7D0491-04 [ICS,6]; CO7D0209-52 [ICS,6]; A61F0003-10 [ICS,6]; A61F0003-10 [ICS,6]; A61F0009-10 [ICS,6]; A61F0009-10 [ICS,6]; A61F0009-10 [ICS,6]; A61F0009-10 [ICS,6]; A61F0009-10 [ICS,6]; CO7D0495-00 [ICL,6]; CO7D0495-00 [ICL,6]; CO7D0495-01 [ICL,6]; CO7D0495-00 [ICL,6]; CO7D0495-00 [ICL,6]; CO7D0491-04 [ICL,6]; CO7D0491-00 [ICL,6]; CO7D0491-04 [ICL,6]; CO7D0491-04 [ICL,6]; CO7D0491-04 [ICL,6]; CO7D0491-04 [ICL,6]; CO7D0491-04 [ICL,6]; CO7D0491-04 [ICL,6]; A61K0031-427 [ICA]; A61K0031-427 [ICA]; A61K0031-427 [ICA]; A61K0031-427 [ICA]; A61K0031-427 [ICA]; A61K0031-427 [ICA]; A61K0031-452 [ICA]; A61K0031-452 [ICA]; A61K0031-452 [ICA]; A61K0031-695 [ICA]; A61K0031-690 [ICA]; A61K0031-690 [ICA]; A61K0031-690 [ICA]; A61F0003-00 [ICA]; A61F003-00 [ICA]
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AB Title compds. [I; Q = substituted aryl, heteroaryl; Z, X = C, CH, CH2, N, B 1tte compds. [t; Q = substituted aryl, heteroaryl; Z, X = C, CH, CHZ, N, O, S; X1 = NRa, CHZ, O, S; dotted lines = bond, null; both dotted lines are not simultaneously bonds; R1 = H, halo, alkoxy, alkylthio, alkyl, CF3, NHZ, alkylamino, dialkylamino, NOZ, CN, CO2H, carboxyalkyl, alkenyl, alkynyl; Ra, Rb = H, alkyl; Y = CH(OH), null; R2R3 = atoms to form a 5-6 membered ring containing 0-3 heteroatoms and 0-2 double bonds; R4 = COA; A = NRdRd, NRaCH2CH2ORa, N-heterocyclyl; Rd = H, alkyl, alkoxy, aryl, (substituted) aryl, heteroaryl; Rc = H, CO2Ra, ORa, SRa, NRaRa; n = 1-3], were prepared for treatment of diabetes, insulin resistance, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, cataracts, hyperglycemia, hypercholesterolemia, diabetic retinopathy, cataracts, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, byperlipidemia, atherosclerosis, or tissue ischemia (no data). Thus, 6H-thieno(2,3-blpyrrole-5-carboxylic acid and (3S)-amino-1-((3R,4S)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-4-phenylbutan-1-one were coupled using 4-(dimethylaminop)pyridine, 1-hydroxybenzotriazole hydrate and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in CH2Cl2/DMF to give 6H-thieno[2,3-blpyrrole-5-carboxylic acid [(1S)-benzyl-3-((3R,4S)-dihydroxypyrrolidin-1-yl-)-2R-hydroxys-1-ay-consyllamide

oppyrnote-3-catnoxynic actu (Ira-9-etta)-1-3-(1-8-a)-4-dinyu doxypyrnot y)|-(2R)-hydroxy-3-oxopropyl)amide.

Fyrrolylcarboxamide fused prepn glycogen phosphorylase inhibitor, thienopyrrolecarboxamide prepn antidiabetic; diabetes insulin resistance diabetic neuropathy treatment fused pyrrolecarboxamide; diabetic nephropathy retinopathy cataract hyperglycemia hypercholesterolemia hypertension treatment pyrrolecarboxamide; hyperinsulinemia hyperlipidemia atherosclerosis tissue chemia treatment fused pyrrolecarboxamide

IT Ischemia (cardiac, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

IT Antiobesity agents a2-Adrenoceptor antagonists b-Adrenoceptor agonists (coadministration; preparation of fused pyrrolylcarboxamides as glycogen

phosphorylase inhibitors)

Sulfonylureas RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

IT Kidney, disease (diabetic nephropathy, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

(diabetic neuropathy, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

1156-19-0, Tolazamide 2295-31-0D, Thiazolidinedione, derivs. 1156-19-0, Tolazamide 2295-31-0D, Thiazolidinedione, derivs. 7440-62-2D, Vanadium, complexes 9004-10-8, Insulin, biological studies 9004-10-8D, Insulin, analogs 10238-21-8, Gilbenclamide 12179-36-1D, Pervanadyl (VO(02)+), complexes 23602-78-0, Benfluorex 28299-33-4D, Imidazoline, derivs. 29094-61-9, Glipizide 37353-31-4, Vanadate 51037-30-0, Acipimox 51110-01-1D, Somatostatin, analogs 54870-28-9, Meglitinide 56180-94-0, Acarbose 66529-17-7, Midaglizole 72432-03-2, Miglitol 74772-77-3, Ciglitazone 75358-37-1, Linogliride 79944-58-4, Glazoxan 80879-63-6, Emiglitate 83480-29-9, Voglibose 86615-96-5, BRL35135 88431-47-4, Clomoxir 89197-32-0, Efaroxan 90505-66-1, Ro 16-8714 90730-96-4, BRL37344 93479-97-1, Glimepiride 97322-87-7, Troulitazone 104343-331-MDL-25637 105182-45-4, Flumaroxan 16-8714 90730-96-4, BRL3.7344 93479-97-1, Glimepiride 97322-87-7, Troglitazone 104343-33-1, MDL-25637 105182-45-4, Fluparoxan 105816-04-4, Nateglinide 106612-94-6, Human GLP-1 (-7-37) 107444-51-9, Rat GLP-1(7-36)amide 109229-58-5, Englitazone 110605-64-6, Isaglidole 111025-46-8, Pioglitazone 109229-58-5, Englitazone 122370-73-4, Rosiglitazone 122575-28-4, Naglivan 122830-14-2, Deriglidole 124083-20-1, Etomoxir 127214-23-7, Camiglibose 130714-47-5, WAG 994 133107-64-9, Insulin lispro 135062-02-1, Repaglinide 138908-40-4, CL 316243 141200-24-0, Darglitazone 141758-74-9, AC2993 187887-46-3, Symlin 395214-16-1 181730-14-9, AC2393 18178-140-3, Symina 395214-16-1 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors) 9001-42-7, a-Gilucosidase 9025-82-5, Phosphodiesterase

TT 332098-11-0P 332098-12-1P 332098-13-2P 332098-14-3P 332098-15-4P 332098-16-5P 332098-17-6P 332098-18-7P 332098-19-8P 332098-20-1P 332098-22-3P 332098-23-4P 332098-29-6P 332098-26-7P 332098-27-8P 332098-28-9P 332098-29-0P 332098-30-3P 332098-31-4P 332098-32-5P 332098-33-6P 332098-34-7P 332098-35-6P 332098-35-6P 332098-35-6P 332098-35-6P 332098-35-6P 332098-35-0P 332098-45-9P 332098-45-9P 332098-45-0P 332098-45-0P 332098-45-0P 332098-46-IP 332098-47-2P 332098-48-3P 332098-49-4P 332098-50-7P 332098-52-9P 332098-54-IP 332098-55-2P 332098-57-4P 332098-59-6P 332098-61-0P 332098-63-2P 332098-65-4P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

Eve. disease

eye, uscasse (diabetic retinopathy, treatment; preparation of fused pyrrolylcarboxamide as glycogen phosphorylase inhibitors)

(fatty acid exidation inhibitors coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

Gluconeogenesis

(inhibitors coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

Heart, disease

(ischemia, treatment; preparation of fused pyrrolylearboxamides as glycogen phosphorylase inhibitors)

Anti-ischemic agents

Anticholesteremic agents Antidiabetic agents

Antihypertensives

Drug delivery systems

Human

Hypolipernic agents
(preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

IT Atherosclerosis

Cataract

Diabetes mellitus

Hypercholesterol Hyperglycemia

Hypertension

Hypertriglyceridemia Ischemia

(treatment; preparation of fused pyrrolylcarboxamides as glycogen

phosphorylase inhibitors)

IT Hyperlipidemia
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treatment; preparation of fused pyrrolylcarboxamides as glycogen
phosphorylase inhibitors)
IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(g. PPAR-g agonists coadministration; preparation of fused
pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
IT 9007-92-5, Glucagon, biological studies 106602-62-4, Amylin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists coadministration; preparation of fused pyrrolylcarboxa
glycogen phosphorylase inhibitors)
IT 56-03-11D, Biruanide derivs. 64-77-7. Tolbutamide 94-20-2.

56-03-1D, Biguanide, derivs. 64-77-7, Tolbutamide 94-20-2, Chloropropamide 114-86-3, Phenformin 458-24-2, Fenfluramine 657-24-9, Metformin 692-13-7, Buformin 968-81-0, Acetohexamide

IT 637-81-0, Azidoacetic acid ethyl ester 1066-54-2, (Trimethylsilyl)acetylene 1126-09-6, Piperidine-4-carboxylic acid ethyl ester 4530-18-1, Boc-DL-Phenylalanine 6030-36-0, 4-Methylthiophene-2-carboxaldehyde 7283-96-7, 5-Chlorothiophene-2-carboxaldehyde 13679-70-4, 5-Methyl-2-thiophenecarboxaldehyde 13734-34-4, Boc-L-Phenylalanine 14345-97-2, 2-Chloro-3-methylthiophene Boc-L-renyusanine 1434-3-7-1, 2-L.nioro-a-menyuniopinen 17186-3-1 18791-75-8, 4-Bromothiophene-2-carboxaldehyde 21508-19-0, 5-Chlorofuran-2-carboxaldehyde 21921-76-6, 4-Bromo-2-furaldehyde 24445-35-0 29669-49-6, 5-Fluorothiophene-2-carboxaldehyde 31486-85-8, Thieno(2,3-bliphiophene-2-carboxaldehyde 35357-56-3, 6H-Thieno(2,3-blipytrole-5-carboxylic acid ethyl ester 39793-31-2, 4H-Thieno(3,2blpyrrole-5-carboxylic acid ethyl ester 39793-31-2, 4H-Thieno[1,2-b]pyrrole-5-carboxylic acid ethyl ester 39793-31-2, 4H-Thieno[1,2-b]pyrrole-5-carboxylic acid 51836-29-8, 6H-Thieno[2,3-b]pyrrole-5-carboxylic acid ethyl ester 57500-51-3, 4-Chlorothiophene-2-carboxaldehyde 58963-45-4, 2-Formyl-6H-thieno[2,3-b]pyrrole-5-carboxylic acid 5998-27-9, 2-Formyl-4H-thieno[1,3-b]pyrrole-5-carboxylic acid ethyl ester 62023-60-3, (2R,3S)-3-Benzyloxycarbonylamino-2-hydroxy-4-phenylbutyric acid 80709-83-7, 2-Bromo-6H-thieno[2,3-b]pyrrole-5-carboxylic acid 80709-83-7, 2-Bromo-6H-thieno[2,3-b]pyrrole-5-carboxylic acid ethyl ester 19545-55-0, 2-Bromo-6H-thieno[2,3-b]pyrrole-5-carboxylic acid ethyl ester 105181-72-4, (2R,3S)-3-terr-Butoxylic acid ethyl ester 105181-72-4, (2R,3S)-3-terr-Butoxylic acid ethyl ester 105181-72-5, 2-Formyl-4H-furo[3,2-b]pyrrole-5-carboxylic acid ethyl ester 19188-80-8
RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of fused pyrrolylcarboxarmides as glycogen phosphorylase (preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

65782-04-9P, 5-Chloro-4-methylthiophene-2-carboxaldehyde 238749-54-7P, 2-Methyl-4H-thieno[3,2-b]pyrrole-5-carboxylic acid ethyl ester 332098-79-0P 332098-81-4P 332098-83-6P, 2-Bromo-6H-thieno[2,3-b]pyrrole-5-carboxylic acid 332098-85-8P, 2-Methyl-6H-thieno[2,3-b]pyrrole-5-carboxylic acid ethyl ester 332098-87-0P, 2-Methyl-6H-thieno[2,3-b]pyrrole-5-carboxylic acid 332098-93-8P 332098-91-6P 332098-93-8P 332098-95-0P 332098-97-2P 332098-99-4P 332099-01-1P, 2-Chloro-6H-thieno[2,3-b]pyrrole-5-carboxylic acid ethyl ester 332099-03-3P, 2-Chloro-6H-thieno[2,3-b]pyrrole-5-carboxylic acid ethyl ester 332099-07-PP, 2,4-Dichloro-6H-thieno[2,3-b]pyrrole-5-carboxylic acid ethyl ester 332099-07-PP, 2-Bromo-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-11-3P, 2-Bromo-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-11-3P, 2-Bromo-4H-thieno[3,2-b]pyrrole-5-carboxylic acid IT 65782-04-9P. 5-Chloro-4-methylthiophene-2-carboxaldehyde 238749-54-7P. acid 332099-19-99; 2-Bromo-4H-thieno[3,2-b]pyrrole-3-carboxylic acid 332099-13-99, 2-Bromo-4H-fur[0]3,2-b]pyrrole-5-carboxylic acid 332099-14-6P, 2-Methyl-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-16-8P, 2-Cyano-6H-thieno[2,3-b]pyrrole-5-carboxylic acid 332099-10-9 332099-20-4P 332099-22-6P, 2-Fluoro-4H-thieno[3,2-b]pyrrole-5-carboxylic acid ethyl ester 332099-24-8P, 2-Fluoro-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-26-0P,

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(preparation of fused pyrrolylcarboxamides as glycogen phosphorylase THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD (1) Esteve, L; ES 2081747 A 1996 CAPLUS (2) Hitzel, V; US 4325963 A 1982 CAPLUS (3) Pfizer, EP 0846464 A 1998 CAPLUS L34 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2003:570833 CAPLUS << LOGINID::20070124>> MBER: 139:111682

Combined use of a GLP-1 compound DOCUMENT NUMBER: and a modulator of diabetic late complications
INVENTOR(S): Knudsen, Lotte Bjerre; Selmer, Johan
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION: KIND DATE APPLICATION NO. DATE PATENT NO.

WO 2003059372 A2 20030724 WO 2002-DK888 20021220 <−
WO 2003059372 A3 20040325

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SS, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

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EP 1461070 A2 20040929 EP 2002-787467 20021220

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JP 2005516968 T 20050609 JP 2003-559533 20021220

PRIORITY APPLN. INFO: DK 2002-760 A 200210219

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DK 2001-1969 A 20011229 WO 2003059372 A2 20030724 WO 2002-DK888 20021220 <--20021220
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IN Knudsen, Lotte Bjerre; Selmer, Johan

PA Novo Nordisk A/S, Den. PCT Int. Appl., 22 pp. CODEN: PIXXD2 DT Patent LA English IC ICM A61K038-00 CC 1-10 (Pharmacology) Section cross-reference(s): 2, 63
FAN.CNT I PATENT NO. KIND DATE APPLICATION NO. DATE PI WO 2003059372 A2 20030724 WO 2002-DK888 20021220 <--O 2003059372 A3 20040325 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, WO 2003059372 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

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use); BIOL (Biological study); USES (Uses)
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IT 525-66-6, Propranolol 13523-86-9, Pindolol 26839-75-8, Timolol
29122-68-7, Atenolol 37517-30-9, Acebutolol 42200-33-9, Nadolol
51384-51-1, Metoprolol 62571-86-2, Captopril 75847-73-3, Enalapril
76547-98-3, Lisinopril 81147-92-4, Esmolol 83647-97-6, Spirapril
85441-61-8, Quinapril 86541-75-5, Benazepril 8733-19-5, Ramipril
87679-37-6, Trandolapril 89371-37-9, Imidapril 89750-14-1D,
GLP-1, analogs or fragments 98048-97-6, Fosinopril
107133-36-8, Perindopril erbumine 114798-26-4, Losartan 135038-57-2,
Alatriopril 136087-85-9, Fidarestat 137862-53-4, Valsartan
138402-11-6, Irbesartan 141732-76-5, Exendin-4 141732-76-5D,
Exendin-4, derivs. 169939-94-0, Ly 333531
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(combined use of a GLP-1 compound and a modulator of
           use); BIOL (Biological study); USES (Uses)
          diabetic late complications)
9015-82-1, Angiotensin-converting enzyme 9028-31-3, Aldose reductase
141436-78-4, Protein kinase C
          RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
   (inhibitors; combined use of a GLP-1 compound and a modulator of diabetic late complications)

134 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2003:320036 CAPLUS <<LOGINID::20070124>>
   DOCUMENT NUMBER:
                                                                                   138:338498
                                          Preparation of human glucagon-like-peptide-1 mimics and their use in the treatment of diabetes
 and their use in the treatment of diabetes
and related conditions
INVENTOR(S): Natarajan, Sesha I.; Bastos, Margarita M.;
Bernatowicz, Michael S.; Mapelli, Claudio; Lee, Ving;
Ewing, William R.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
COCUMENT TARR
   DOCUMENT TYPE:
                                                               Patent
English
  LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:
           PATENT NO.
                                                               KIND DATE
                                                                                                                  APPLICATION NO.
                                                                  A2 20030424
           WO 2003033671
                                                                                                               WO 2002-US33386
           WO 2003033671
                                                                    A3 20051229
                 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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4C206/ZA33; 4C206/ZA36; 4C206/ZA42; 4C206/ZA43; 4C206/ZA36; 4C206/ZC42

4C206/ZC20; 4C206/ZC35; 4C206/ZC42

US 2003144206 IPC1 A61K0038-26 [ICM,7]; A61K0031-401 [ICS,7]

IPCR A61K0031-401 [LC°]; A61K0031-401 [LA]; A61K0038-26

[LC°]; A61K0038-26 [LA]

NCL 514/012.000, 514/423.000

AB Methods and uses for treatment of diabetic late complications comprising
     administration of a GLP-1 compound and a modulator of
       diabetic complications.
ST GLP1 diabetes late complication therapy; glucagon like peptide I analog fragment antidiabetic
 IT Angiotensin receptor antagonists
     Antihypertensives
     Human
       Hypertension
     Protein sequences
     bl-Adrenoceptor antagonists
bl-Adrenoceptor antagonists
(combined use of a GLP-1 compound and a modulator of
          liabetic late complications)
IT Kidney, disease
        (diabetic nephropathy; combined use of a GLP-
1 compound and a modulator of diabetic late complications)
      Nerve, disease
(diabetic neuropathy; combined use of a GLP-1
         compound and a modulator of diabetic late complications)
       Eye, disease
        (diabetic retinopathy; combined use of a GLP-1 compound and a modulator of diabetic late complications)
 IT Gene, animal
    Netter, annua
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(glp-1; combined use of a GLP-1
compound and a modulator of diabetic late complications)

    Diabetes mellitus
    (non-insulin-dependent; combined use of a GLP-1
    compound and a modulator of diabetic late complications)
    Antidiabetic agents

     Drug delivery systems
(oral; combined use of a GLP-1 compound and a
         modulator of diabetic late complications)
      Drug delivery systems
(parenterals; combined use of a GLP-1 compound and a
          nodulator of diabetic late complications)
     RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
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4C206/ZA33: 4C206/ZA36: 4C206/ZA42: 4C206/ZA81:

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ZA 2004002846 A 20050816 ZA 2004-2846 20040415
PRIORITY APPLN. INFO: US 2001-342015P P 20011018
WO 2002-US33386 W 20021018
OTHER SOURCE(S): MARPAT 138:338498
  OTHER SOURCE(S): MARPAT 138:338498
AN 2003:320036 CAPLUS <<LOGINID::20070124>>
DN 138:338498
   ED Entered STN: 25 Apr 2003
  TI Preparation of human glucagon-like-peptide-1 mimics and their use in the treatment of diabetes and related conditions
   IN Natarajan, Sesha L; Bastos, Margarita M.; Bernatowicz, Michael S.;
Mapelli, Claudio; Lee, Ving; Ewing, William R.
PA Bristol-Myers Squibb Company, USA
  SO PCT Int. Appl., 153 pp.
CODEN: PIXXD2
LA English
IC ICM
   DT Patent
             ICM CI2N
  CC 34-3 (Amino Acids, Peptides, and Proteins)
           Section cross-reference(s): 1, 63
  FAN.CNT 2
PATENT NO.
                                                                  KIND DATE
                                                                                                                  APPLICATION NO.
                                                                                                                                                                                               DATE
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                                                                        A2 20030424 WO 2002-US33386
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BR 2002013377 A 20060523 BR 2002-13377 20021018
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PRAI US 2001-342015P P 20011018
WO 2002-US33386 W 20021018
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        WO 2003033671 ICM C12N

IPCI C12N [ICM,7]

IPCR A61K0038-00 [I,C*]; A61K0038-00 [I,A]; A61K0038-26

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ECLA C07K014/605

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NO 2004001203 IPCI C07K0014-605 [ICM,7]; C07K0014-435 [ICM,7,C*];
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ECLA C0*[C0*]-405 [LC*]; C0*[C0*]-435 [LC*]; A61K00

ZA 2004002845 [PCR A61K0038-00 [N.C*]; C0*[K0014-435 [LC*]; A61K00
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ZA 2004002846 PPCR A61K0038-00 [N,C°]; C07K0014-435 [LC°]; A61K0038-00
[N,A]; C07K0014-605 [I,A]
ECLA C07K014/605
OS MARPAT 138:338498
 OS MARPAT 138:338498

AB The invention provides novel human glucagon-like peptide-1 (GLP-1) peptide mimics A-Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Xaa6-Xaa7-Xaa8-Xaa9-Y-Z-B [Xaa1-Xaa9 are naturally or non-naturally occurring amino acid residues; Y and Z are amino acid residues which may be substituted; A and B are optionally present; A is H, an amino acid or peptide containing .apprx. 1-15 amino acid residues, an R group [H, (cyclo)alkyl, cycloxalkylalkyl, heterocyclyl, heterocycloalkyl, (heteroparylarylarylalkyl, aryloxyalkyl, heteroarylalkyl, or heteroaryloxyalkyl], an RCO (amide) group, a carbamate group, a urea, a sulfonamido, or an aminosulfonyl group; B is OH, alkoxy, etc., an amino or amino acid residue, or a nentide containing from 1-15 amino
              etc., an amino or amino acid residue, or a peptide containing from 1-15 amino acid residues, terminating at the C-terminus as a carboxamide, ester, carboxyl, or an amino alc.] that mimic the biol. activity of the native GLP-1 peptide and thus are useful for the treatment or
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     JP 2005514337
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CN 1630709
EP 1572892
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prevention of diseases or disorders associated with GLP activity. These chemical-modified peptides stimulate insulin secretion in type II diabetics and produce other beneficial insulinotropic responses, while exhibiting increased stability to proteolytic cleavage making them ideal therapeutic candidates for oral or parenteral administration. A method of preparing the polypeptides comprises replacing the message sequence of the polypeptide with a variant message sequence capable of inducing receptor mediated signal transduction. An example is claimed peptide H-AEGTFTSD-Bip(2-Et)-Bip(2-Me)-NH2 (Bip = biphenylalanine residue).

ST glucagon like peptide mimic prepn treatment diabetes

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of human glucagon-like-peptide-1 mimics) (antiatherosclerotics; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions) IT Kidney, disease
(diabetic nephropathy; preparation of human glucagon-like-peptideI mimics for use in treatment of diabetes and related

conditions)

IT Nerve, disease

(diabetic neuropathy; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

Eye, disease

(diabetic retinopathy; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

Metabolic disorders

(metabolic syndrome X; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

IT Antidiabetic agents

Antihypertensives

Antiobesity agents

Atherosclerosis
Diabetes mellitus

Hyperglycemia

Hypertension Hypertriglyceridemia

Hypolipemic agents
Obesity
Wound healing
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

IT Hyperlipidemia RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation of human glucagon-like-peptide-1 mimics for use in treatment of liabetes and related conditions)

IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

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(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

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516518-33-5P 516518-31-7P 516518-30-PP 516518-30-PP 516518-30-PP

516518-31-3P 516518-31-7P 516518-30-PP 516518-30-PP 516518-30-PP

516519-32-PP 516518-31-PP 516518-30-PP 516518-30-PP 516518-30-PP

516519-32-PP 516519-31-PP 516518-30-PP 516518-30-PP 516518-30-PP

516519-32-PP 516519-31-PP 516518-30-PP 516518-30-PP 516518-30-PP

516519-32-PP 5
        L34 ANSWER 5 OF 9 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
       ACCESSION NUMBER: 2003:390202 BIOSIS << LOGINID::20070124>> DOCUMENT NUMBER: PREV200300390202
                                                                       The glucagon-like peptides: A double-edged therapeutic
        TITLE:
       AUTHOR(S): Perry, TracyAnn [Reprint Author]; Greig, Nigel H.
CORPORATE SOURCE: Section of Drug Design and Development, Laboratory of
Neurosciences, Gerontology Research Center, National
                                                          Institute on Aging, National Institutes of Health, 5600
Nathan Shock Drive, Baltimore, MD, 21224, USA
     National Stock Drive, Baltimore, MD, 21224, USA pernyl@grc.nia.nib.gov

SOURCE: Trends in Pharmacological Sciences, (July 2003)

Vol. 24, No. 7, pp. 377-383, print.

ISSN: 0165-6147 (ISSN print).

DOCUMENT TYPE: Article
     General Review; (Literature Review)

LANGUAGE: English

ENTRY DATE: Entered STN: 27 Aug 2003

Last Updated on STN: 27 Aug 2003

AN 2003:390202 BIOSIS <<LOGINID::20070124>>
     AN 2003:390202 BIOSIS < LOGINID::20070124>>>
DN PREV200300390202
T1 The glucagon-like peptides: A double-edged therapeutic sword?.
AU Perry, TracyAnn [Reprint Author]; Greig, Nigel H.
CS Section of Drug Design and Development, Laboratory of Neurosciences, Gerontology Research Center, National Institute on Aging, National Institutes of Health, 5600 Nathan Shock Drive, Baltimore, MD, 21224, USA
     perryt@grc.nia.nih.gov
SO Trends in Pharmacological Sciences, (July 2003) Vol. 24, No. 7,
                  pp. 377-383. print.
ISSN: 0165-6147 (ISSN print).
       DT Article
                  General Review; (Literature Review)
        LA English
     LA English
ED Entered STN: 27 Aug 2003
Last Updated on STN: 27 Aug 2003
AB Glucagon-like peptide-1(7-36)-amide (GLP-1) is an endogenous peptide that is secreted from the gut in response to the presence of food. Recent studies have established that GLP-
                       and its longer-acting analog exendin-4 have multiple
                I and its longer-acting analog exendin-4 nave multiple synergistic effects on glucose-dependent, insulin secretion pathways of the pancreatic beta-cell and on plasticity in neuronal cells. Recent interest has focused on the development of these peptides as a novel therapeutic strategy for non-insulin-dependent (type 2) diabetes mellitus and associated neuropathy. This is with a view to developing lead compounds, based on neurotrophic action, for central and peripheral
```

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (preparation of human glucagon-like-peptide-1 mimics for use in treatment of

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516521-28-IP 516521-29-2P 516521-30-5P 516521-31-6P 516521-32-7P 516521-33-8P 516521-34-9P 516521-35-0P 516521-36-IP 516521-37-2P 516521-38-3P 516521-39-4P 516521-40-7P 516521-41-8P 516521-42-9P 516521-43-P 516521-44-IP 516521-45-2P 516521-53-2P 516521-54-3P 516521-54-P
       RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
       (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
           (preparation of human glucagon-like-peptide-1 mimics for use in treatment of
            diabetes and related conditions)
 IT 150-46-9, Triethyl borate 1973-22-4, 1 Bromo 2 ethylbenzene 4326-36-7 16419-60-6, o Tolylboronic acid 93267-04-0 516521-49-6
      10419-60-6, o Tolylboronic acid 93267-04-0 510521-49-6
RL: RCT (Reactant or reagent)
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)
90002-36-1P, 2 Ethylphenylboronic acid 112766-18-4P 516521-46-3P 516521-47-4P 516521-48-5P 516521-50-9P 516521-51-0P
         RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
       (Reactant or reagent)
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of
           diabetes and related conditions)
     diabetes and related conditions)
51-64-9, Dexamphetamine 94-20-2, Chloropropamide 122-09-8, Phentermine
637-07-0, Clofibrate 657-24-9, Metformin 9004-10-8, Insulin,
biological studies 10238-21-8, Glyburide 14838-15-4,
Phenylpropanolamine 21187-98-4, Gliclazide 22232-71-9, Mazindol
25812-30-0, Gemfibrozil 29094-61-9, Glipizide 49562-28-9, Fenofibrate
56180-94-0, Acarbose 72432-03-2, Miglitol 75330-75-5, Lovastatin
79902-63-9, Simwastatin 8109-33-70, Pravastatin 39479-97-1,
Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4,
Topiramate 97322-87-7, Troglitazone 105816-04-4, Nateglinide
10650-56-0, Siburamine 111025-46-8, Pioditazone 122320-73-4.
      Topiramate 9/32/2-87-7, Troghtazone 105816-04-4, Nateglinide 10650-56-0, Siburamine 111025-64-8, Pioglitazone 12320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 141750-63-2, Nisvastatin 141758-74-9, AC 2993 144288-97-1, TS-962 145599-86-6, Cerivastatin 152755-31-2, LY295427 159183-92-3, L750355 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 196808-45-4 199113-98-9
      199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 258345-41-4, GW-409544 262352-17-0, CP 529414 282526-98-1, ATL-962 287714-41-4 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0,
       KAD1129 335149-17-2, ARHO39242 335149-23-0, NVPDPP-728A 335149-25-
      CP331648 430433-17-3, Glipyride 444069-80-1, Axokine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)
     degenerative disorders such as stroke and Alzheimer's disease in addition to the peripheral neuropathy associated with type 2 diabetes mellitus. Here, we address recent advances in the biological action of GLP-1 and its related analogs.
CC Cytology - Animal 02506

Biochemistry studies - Proteins, peptides and amino acids 10064

Biochemistry studies - Carbohydrates 10068
     Pathology - Therapy 12512
Metabolism - Metabolic disorders 13020
Cardiovascular system - Blood vessel pathology 14508
Endocrine - General 17002
      Endocrine - Pancreas 17008
     Endocrine - Pancreas 17008
Endocrine - Neuroendocrinology 17020
Nervous system - Physiology and biochemistry 20504
Nervous system - Pathology 20506
Pharmacology - General 22002
 IT Major Concepts
          Endocrine System (Chemical Coordination and Homeostasis); Nervous
       System (Neural Coordination); Pharmacology
Parts, Structures, & Systems of Organisms
          beta cells: endocrine system; neuronal cells: nervous system
           Alzheimer's disease: behavioral and mental disorders, nervous system
          Alzheimer Disease (MeSH)
       Discases
          diabetic neuropathy: endocrine disease/pancreas, metabolic disease,
          nervous system disease
Diabetic Nephropathics (MeSH)
       Diseases
          stroke: nervous system disease, vascular disease
          Cerebrovascular Disorders (MeSH)
       Diseases
type 2 diabetes mellitus: endocrine disease/pancreas,
            netabolic disease
Diabetes Mellitus, Non-Insulin-Dependent (MeSH)
 IT Chemicals & Biochemicals
       glucagon-like peptide-1(7-36)-amide; glucose; insulin
Miscellaneous Descriptors
 drug development
RN 118549-37-4 (glucagon-like peptide-1(7-36)-amide)
     50-99-7Q (glucose)
58367-01-4Q (glucose)
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9004-10-8 (insulin)

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L34 ANSWER 6 OF 9 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

DUPLICATE 1

ACCESSION NUMBER: 2001:506591 BIOSIS <<LOGINID::20070124>> DOCUMENT NUMBER: PREV200100506591

TITLE: Urinary exerction of glucagon-like peptide 1 (GLP -1) 7-36 arnide in human type 2

(non-insulin-dependent) diabetes mellitus.

AUTHOR(S): Lugari, R. [Reprint author]; Ugolotti, D.; Dei Cas, A.; Barilli, A. L.; lotti, M.; Marani, B.; Orlandini, A.; Gnudi, A.; Zandomeneghi, R.

CORPORATE SOURCE: Cattedra di Endocrinologia, Via Gramsci 14, 43100, Parma, Italy endoparm@ipruniv.cce.unipr.it

SOURCE: Hormone and Metabolic Research, (September, 2001) Vol. 33, No. 9, pp. 568-571. print.

CODEN: HMMRA2. ISSN: 0018-5043.

DOCUMENT TYPE: Arricle

LANGUAGE: English

ENTRY DATE: Entered STN: 31 Oct 2001

Last Updated on STN: 23 Feb 2002

AN 2001:506591 BIOSIS <<LOGINID::20070124>> DN PREV200100506591

TI Urinary excretion of glucagon-like peptide 1 (GLP-1)

7-36 arnide in human type 2 (non-insulin-dependent) diabetes mellitus.

AU Lugari, R. [Reprint author]; Ugolotti, D.; Dei Cas, A.; Barilli, A. L.; lotti, M.; Marani, B.; Orlandini, A.; Gnudi, A.; Zandomeneghi, R.

CS Cattedra di Endocrinologia, Via Gramsci 14, 43100, Parma, Italy endoparm@ipruniv.cce.unipr.it

SO Hormone and Metabolic Research, (September, 2001) Vol. 33, No. 9, pp. 568-571, print.

CODEN: HMMRA2. ISSN: 0018-5043.

DT Article

LA English

ED Entered STN: 31 Oct 2001

Last Updated on STN: 23 Feb 2002

AB The urinary excretion of insulinotropic glucagon-like peptide 1 (
GLP-1) was investigated as an indicator of renal tubular integrity in 10 healthy subjects and in 3 groups of type 2 diabetic patients with different degrees of urinary albumin excretion rate. No significant difference emerged between the groups with respect to age of the patients, known duration of diabetes, metabolic control, BMI, or residual beta-cell pancreatic function. Endogenous creatinine clearance was significantly reduced under conditions of overt diabetic nephropathy, compared with normo and mic
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RN 60-27-5 (creatinine)
ANSWER 7 OF 9 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights
 reserved on STN
ACCESSION NUMBER: 96034762 EMBASE <<LOGINID::20070124>>
ACCESSION NUMBER: 96034762 EMBASE <LOGINID::20070124:

DOCUMENT NUMBER: 1996034762

TITLE: Gastric emptying, glucose responses, and insulin secretion after a liquid test meal: Effects of exogenous glucagon-like peptide-1 (GLP-1)-(7-36) amide in type 2 (noninsulin-dependent) diabetic patients.

AUTHOR: Willms B.; Werner J.; Holst J.J.; Orskov C.; Creutzfeldt W.; Nauck M.A.
CORPORATE SOURCE: Department of Medicine, Ruhr-University Bochum,
Knappschafts-Krankenhaus, In der Schornau 23-25,44892
                         Bochum, Germany
Journal of Clinical Endocrinology and Metabolism, (
1996) Vol. 81, No. 1, pp. 327-332.

ISSN: 0021-972X CODEN: JCEMAZ
ISSN: 0021-972X CODEN: JCEMAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 1996
Last Updated on STN: 20 Feb 1996
AN 96034762 EMBASE <<LOGINID::20070124>>
DN 1996034762
 DN 1996034762
TI Gastric emptying, glucose responses, and insulin secretion after a liquid test meal: Effects of exogenous glucagon-like peptide-1 (GLP-1)-(7-36) amide in type 2 (noninsulin-dependent) diabetic
patients.

AU Willms B.; Werner J.; Holst J.J.; Orskov C.; Creutzfeldt W.; Nauck M.A.

CS Department of Medicine, Ruhr-University Bochum, Knappschafts-Krankenhaus,
      In der Schomau 23-25.44892 Bochum, Germany
In der Schomau 23-25,44892 Bochum, Germany
SO Journal of Clinical Endocrinology and Metabolism, (1996) Vol.
81, No. 1, pp. 327-332.
ISSN: 0021-972X CODEN: JCEMAZ
CY United States
DT Journal; Article
FS 003 Endocrinology
                  Drug Literature Index
      037
  LA English
SL English
ED Entered STN: 20 Feb 1996
      Last Undated on STN: 20 Feb 1996
 AB The aim of the study was to investigate whether inhibition of gastric
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(p<0.01). Urinary excretion of GLP-1 was
        (p<0.01). Unnary exerction of cult-1 was significantly higher in normoalbuminuric patients compared to controls (490.4+211.5 vs. 275.5+132.1 pg/min; p<0.05), with further increase under incipient diabetic nephropathy conditions (648.6+-305 pg/min; p<0.01). No significant difference resulted, in contrast, between
        macroproteinuric patients and non-diabetic subjects. Taking all patients examined into account, a significant positive relationship emerged between
        examined into account, a significant postative retrainisting heringed between urinary GLP-1 and creatinine clearance (p=0.004). In conclusion, an early tubular impairment in type 2 diabetes would occur before the onset of gloinerular permeability alterations. The tubular dysfunction seems to evolve with the development of persistent microalbuminuria. Finally, the advanced tubular involvement, in terms of
       microaluminum. Finally, the advanced unbust involvement, in te-
urinary GLP1 excretion, under overt diabetic nephropathy
conditions would be masked by severe concomitant glomerular dam
the coexistence of both alterations resulting in a peptide excretion
similar to control subjects.
CC Biochemistry studies - Proteins, peptides and amino acids 10064
Metabolism - Metabolic disorders 13020
Urinary system - Pathology 15506
Endocrine - General 17002
        Endocrine - Pancreas 17008
        Major Concepts
Clinical Endocrinology (Human Medicine, Medical Sciences); Nephrology
(Human Medicine, Medical Sciences)
            diabetic nephropathy: endocrine disease/pancreas, metabolic disease, urologic disease
            Diabetic Nephropathies (MeSH)
            type 2 diabetes mellitus: endocrine disease/pancreas,
             metabolic disease, non-insulin-dependent diabetes mellitus
Diabetes Mellitus, Non-Insulin-Dependent (MeSH)
Diabetes Mellitus, Non-Insulin-Dependent (MeSH)
IT Chemicals & Biochemicals
creatinine; glucagon-like peptide 1: renal tubular integrity indicator;
glucagon-like peptide 1 7-36 amide [GLP-1 7-36
amide]: urinary excretion
IT Miscellaneous Descriptors
glomerular permeability
ORGN Classifier
            Hominidae 86215
        Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
        Organism Nam
                     man: patient
```

. Animals, Chordates, Humans, Mammals, Primates, Vertebrates

emptying of meals plays a role in the mechanism of the blood glucose-lowering action of glucagon-like peptide-1-(7-36) amide [GLP-1-(7-36) amide] in type 2 diabeties. Eight poorly controlled type 2 diabetic patients (age, 58 ± 6 yr, body mass index, 30.0 ± 5.2 kg/m², hemoglobin A(1c), 10.5 ± 1.2%) were studied in the fasting state (plasma glucose, 11.1 ± 1.1 mmol/L). A liquid meal of 400 mL containing 8% amino acids and 50 g sucrose (327 Kcal) was administered at time zero by a nasogastric tube. Gastric volume was determined by a dye dilution technique using phenol red. In randomized order, GLP-1-(7-36) amide (1.2 pmol/kg·min; Saxon Biochemicals) or placebo (0.9% NaCl with 1% human serum albumin) infused between -30 and 240 min. In the control experiment, gastric emptying was completed within 120 min, and plasma glucose, insulin, C-peptide, GLP-1-(7-36) amide, and glucagon concentrations transiently increased. With exogenous GLP-1-(7-36) amide (plasma level, apprx. 70 pmol/L), gastric volume remained constant over the period it was measured (120 min, P < 0.0001 vs. placebo), and plasma glucose fell to normal fasting values (5 4 ± 0.7 mmol/L) within 3-4 h, whereas insulin was stimulated in most, but not all, patients, and glucagon remained at the basal level or was slightly suppressed. In conclusion, GLP-1-(7-36) amide inhibits gastric emptying in type 2 diabetic patients. Together with the stimulation of insulin and the inhibition of glucose-lowering action of GLP-1-(7-36) amide in type 2-diabetic patients when studied after meal ingestion. At the degree observed, inhibition of gastric emptying, however, must be overcome by tachyphylaxis, reduction in dose, or pharmacological interventions so as not to interfere with the therapeutic use of GLP-1-(7-36) amide in type 2-diabetic patients.

CT Medical Descriptors:

insulin release

*non insulin dependent diabetes mellitus: DT, drug therapy

*non insulin dependent empty and the proper storage demands and the proper storage demands and the proper storage demands a

*non insulin dependent diabetes mellitus:
*non insulin dependent diabetes mellitus:
*stomach emptying
adult
aged
article
clinical article
clinical trial
controlled study
diabetic angiopathy: CO, complication
diabetic diet diabetic neuropathy: CO, complication
diabetic neuropathy: CO, complication
diabetic retinopathy

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drug effect
drug mechanism
      glucagon release
       glucose blood level
       hormone inhibition
      human
        hypertension: DT, drug therapy
      intravenous drug administr
      male
      postprandial state
      priority journal
randomized controlled trial
      Drug Descriptors:
       glucagon like peptide 1 [7-36] amide: CM, drug comparisor
       glucagon like peptide 1 [7-36] amide: DT, drug therapy
glucagon like peptide 1 [7-36] amide: PD, pharmacolog
      *glucagon like peptide 1 [7-36] amide: CT, clinical trial
*glucose: EC, endogenous compound
*insulin: EC, endogenous compound
     acarbose: DT, drug therapy
captopril plus hydrochlorothiazide: DT, drug therapy
glibenclamide: DT, drug therapy
isosorbide dinitrate: DT, drug therapy
     metformin: DT, drug therapy
metoprolol: DT, drug therapy
     nifedipine: DT, drug therapy
ntreatpine: D1, ang merapy
placebo: CM, drug comparison
RN (glucagon like peptide 1 [7-36] amide) 119637-73-9; (glucose) 50-99-7,
84778-64-3; (insulin) 9004-10-8; (acarbose) 56180-94-0; (glibenclamide)
10238-21-8; (isosorbide dinitrate) 87-33-2; (metformin) 1115-70-4,
657-24-9; (metoprolol) 37350-58-6; (nifedipine) 21829-25-4
CO Saxon (Germany)
L34 ANSWER 8 OF 9 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights
      reserved on STN
                                                                    DUPLICATE 2
ACCESSION NUMBER: 93286381 EMBASE <<LOGINID::20070124>> DOCUMENT NUMBER: 1993286381
                          Preserved incretin effect in type 1 diabetic patients with
                    end-stage nephropathy treated by combined
heterotopic pancreas and kidney transplantation.
Nauck M.A.; Busing M.; Orskov C.; Siegel E.G.; Talartschik
AUTHOR:
                   J.; Baartz A.; Baartz T.; Hopt U.T.; Becker H.-D.;
Creuzfeld W.

CORPORATE SOURCE: Div. of Gastroenterol/Endocrinology, Department of Medicine, Georg August University, Robert-Koch-Strasse
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(incretin effect). Insulin responses after the oral glucose challenge
       (incretin effect). Insulin responses after the oral glucose challenge were similar in the two patient groups despite systemic venous drainage of the pancreas graft in the pancreas-kidney-transplanted group. In both groups GIP and GLP-1 increased after oral but not after intravenous glucose, and B cell secretory responses were significantly smaller (by 55.2 ± 7.7% and 46.5 ± 12.5%, respectively) with 'isoglycaemic' intravenous glucose infusions. The lack of reduction in the incretin effect in pancreas-kidney-transplanted
        patients, whose functioning pancreas is denervated, indicates a lesser
role for the nervous system and a more important contribution of
         circulating incretin hormones in mediating the enteroinsular axis in man.
CT Medical Descriptors:

*diabetic nephropathy: SU, surgery

*insulin dependent diabetes mellitus

*kidney transplantation
          pancreas transplantation
         article
        clinical article
         controlled study
        human
         Drug Descriptors:
           gastric inhibitory polypeptide: EC, endogenous compound glucagon like peptide 1: EC, endogenous compound
*insulin: EC, endogenous compound

RN (gastric inhibitory polypeptide) 59392-49-3; (glucagon like peptide 1)

89750-14-1; (glucose) 50-99-7, 84778-64-3; (insulin) 9004-10-8
L34 ANSWER 9 OF 9 MEDLINE on STN
ACCESSION NUMBER: 92288534 MEDLINE <<LOGINID::20070124>>
DOCUMENT NUMBER: PubMed ID: 1600330
TITLE: Basal and nurriem-strimulated pancreatic and
                             gastrointestinal hormone concentrations in type-1-diabetic
patients after successful combined pancreas and kidney
transplantation.

AUTHOR: Nauck M A; Busing M; Orskov C; Siegel E G; Talartschik J;
Baartz A; Baartz T; Holzer H; Hopt U T; Ebert R; +

CORPORATE SOURCE: Abteilung Gastroenterologie und Endokrinologie,
Georg-August-Universitat, Gottingen.

SOURCE: The Clinical investigator, (1992 Jan) Vol. 70,
No. 1, pp. 40-8.

Journal code: 9207154. ISSN: 0941-0198.
                              transplantation.
 PUB. COUNTRY: GERMANY: Germany, Federal Republic of
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40,W-3400 Gottingen, Germany
Acta Diabetologica, (1993) Vol. 30, No. 1, pp.
39-45. .
 SOURCE:
                         ISSN: 0940-5429 CODEN: ACDAEZ
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
Oblinternal Medicine
029 Clinical Biochemistry
 LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Oct 1993
 Last Updated on STN: 31 Oct 1993
AN 93286381 EMBASE <<LOGINID::20070124>>
 DN 1993286381
 TI Preserved incretin effect in type 1 diabetic patients with end-stage
nephropathy treated by combined heterotopic pancreas and kidney
       nephropathy treated by comb
 AU Nauck M.A.; Busing M.; Orskov C.; Siegel E.G.; Talartschik J.; Baartz A.;
Baartz T.; Hopt U.T.; Becker H.-D.; Creutzfeldt W.
CS Div. of Gastroenterol/Endocrinology, Department of Medicine, Georg August University, Robert-Koch-Strasse 40,W-3400 Gottingen, Germany SO Acta Diabetologica, (1993) Vol. 30, No. 1, pp. 39-45.

ISSN: 0940-5429 CODEN: ACDAEZ
 CY Germany
DT Journal; Article
FS 003 Endocrinology
006 Internal Medicine
029 Clinical Biochemistry
 LA English
SL English
ED Entered STN: 31 Oct 1993
      Last Updated on STN: 31 Oct 1993
 AB Insulin secretion is stimulated better by oral than by intravenous glucose
     incretin effect). The contribution of the autonomic nervous system to the incretin effect after oral glucose in humans is unclear. We therefore examined nine type I diabetic (insulin-dependent) patients with end-stage nephropathy, studied after combined heterotopic pancreas and
     kidney transplantation, and 7 non-diabetic kidney recipients (matched for creatinine clearance and immunosuppressive medication). The release of gastric inhibitory polyperide (GIP) and glucagon-like peptide 1 (GLP-1) immunoreactivity and B cell secretory responses
      (IR insulin and C-peptide) to oral (50 g) and 'isoglycaemic' intravenous glucose (identical glycaemic profile)were measured by radioimmunoassay.
      The difference in B cell responses between the two tests represents the contribution of the enteroinsular axis to the response after oral glucose
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FILE SEGMENT:
                                                     Priority Journals
  ENTRY MONTH:
                                                            199207
ENTRY MONTH: 19920/

ENTRY DATE: Entered STN: 24 Jul 1992

Last Updated on STN: 24 Jul 1992

Entered Medline: 13 Jul 1992

AN 92288534 MEDLINE <<LOGINID::20070124>>

DN PubMed ID: 1600330
  TI Basal and nutrient-stin
                                                                           lated pancreatic and gastrointestinal horm
11 Dasas and nutrient-sumulated pancreatic and gastrointestinal hormone concentrations in type-1-diabetic patients after successful combined pancreas and kidney transplantation.

AU Nauck M A; Busing M; Orskov C; Siegel E G; Talartschik J; Baartz A; Baartz T; Holzer H; Hopt U T; Ebert R; +

CS Abteilung Gastroenterologie und Endokrinologie, Georg-August-Universitat,
Gottingen.

SO The Clinical investigator, (1992 Jan) Vol. 70, No. 1, pp. 40-8.
SO The Climical investigator, (1992 Jan) vol. Journal code: 9207154. ISSN: 0941-0198.

CY GERMANY: Germany, Federal Republic of DT Journal; Article; (JOURNAL ARTICLE)

A English FS Priority Journals

EM 199207

Descript
 ED Entered STN: 24 Jul 1992
         Last Updated on STN: 24 Jul 1992
Entered Medline: 13 Jul 1992
AB The secretion of pancreatic and gastrointestinal hormones in the basal state and after nutrient stimuli (50 g glucose, 50 g protein, or 30 g triglyceride administered on separate occasions) was assessed in ten
         previously type-1-diabetic patients after successful combined kidney and
         pancreas transplantation (systemic venous drainage). Fasting values were compared to matched non-diabetic kidney-transplanted patients and related to kidney function (endogenous creatinine clearance) and to the type and
         dosage of immunosuppressive medication. In the fasting state, only IR insulin concentrations were higher in pancreas-kidney-transplanted
         patients (by 88%; P = 0.001) than in the kidney graft recipients. There were significant inverse correlations of plasma C-peptide, GIP, and
         gastrin immunoreactivity to endogenous creatinine clearance (kidney function). In response to nutrients, insulin secretion (IR insulin,
       function). In response to nutrients, insulin secretion (IR insulin, C-peptide) was significantly stimulated by glucose, and - to a lesser degree - also by protein. Pancreatic glucagon was suppressed by glucose and stimulated by protein ingestion. GIP was raised after glucose and triglyceride more than after protein (P = 0.0003). GLP-1 immunoreactivity was stimulated by all nutrients, with a tendency towards higher responses to protein and fat (P = 0.06). Gastrin was mainly raised by protein. In conclusion, the overall pattern of
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Journal; Article; (JOURNAL ARTICLE)

DOCUMENT TYPE:

English

LANGUAGE:

pancreatic and gastrointestinal hormone release is normal in patients after combined pancreas-kidney-transplantation, but there are some peculiarities due to (a) systemic venous drainage of the pancreas graft (elevated fasting IR insulin) and (b) impaired kidney function (negative correlation of fasting plasma values to endogenous creatinine clearance for C-peptide, GIP, and gastrin).(ABSTRACT TRUNCATED AT.250 WORDS)

CT Check Tags: Female; Male
Adult
Blood Glucose: ME, metabolism
Diabetes Mellitus, Type 1: BL, blood
Diabetes Mellitus, Type 1: SU, surgery
Diabetic Nephropathies: BL, blood
Diabetic Nephropathies: BL, blood
Diabetic Nephropathies: SU, surgery
Gastrointestinal Hormones: BL, blood
Humans
Kidney Function Tests
*Kidney Transplantation: PH, physiology
Middle Aged
Pancreas Transplantation: PH, physiology
Pancreatic Hormones: BL, blood
Research Support, Non-U.S. Gov't
CN 0 (Blood Glucose); 0 (Gastrointestinal Hormones); 0 (Pancreatic Hormones)